Supplementary Information

Carbonyl-Assisted Reverse Regioselective Cascade Annulation of 2-Acetylenic Ketones Triggered by Ru-Catalyzed C–H Activation

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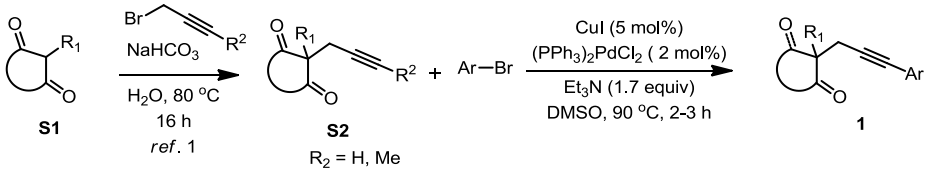
I. General details

***General information*:** Unless otherwise noted, all reagents were used as received from commercial suppliers. Ruthenium catalyst was obtained from Sigma-Aldrich and used without further purification. All reactions were performed under nitrogen atmosphere and in a flame-dried or oven-dried glassware with magnetic stirring. All solvents were dried before use following the standard procedures. Reactions were monitored using thin-layer chromatography (SiO_2). TLC plates were visualized with UV light (254 nm), iodine treatment or using *p*-anisaldehyde stain. Column chromatography was carried out using silica gel (60-120 mesh & 100-200 mesh) packed in glass columns. NMR spectra were recorded at 300, 400, 500, 600 MHz (H) and at 75, 100, 125, 150 MHz (C), respectively. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 and C: δ = 77.16 ppm) as internal standard, and coupling constants (*J*) are given in Hz. HRMS were recorded using ESI-TOF techniques.

II. Experimental procedures and analytical data

IIa. General procedure for the synthesis of 2-acetylenic ketones:



*General procedure for the synthesis of **S1** from 1,3-diketones using Ramachary protocol*: [1]

A solution of aldehyde (3.0 equiv), 1,3-diketone (1.0 equiv) and Hantzsch ester (1.0 equiv) in solvent (0.3M) was added amino acid catalyst (0.05 equiv, 5 mol%) and the reaction mixture was stirred at 25 ^oC for 1 h. After evaporation of the solvent completely, the crude reaction mixture was directly subjected to silica gel column chromatography (hexane–ethyl acetate) to afford product **S1**.

*General procedure for the synthesis of **S2***:[2]

To a vigorous stirred suspension of cyclic diketone **S1** (1 equiv) in water (1 M) was gradually added powdered $NaHCO_3$ (1 equiv). After the frothing had settled, propargyl bromide (2 equiv.) was added and the reaction mixture was stirred at 80 ^oC for 16 hr. Later, The reaction mixture was extracted with CH_2Cl_2 (2 times) and the combined organic solvent was washed with 5% aqueous $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The crude

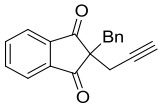
reaction mixture was purified by either recrystallization or column chromatography (EtOAc/hexane) to give acetylenic 1,3-diketones **S2**.

*General procedure for the synthesis of **1**:*[3]

To a solution of 2-acetylenic ketone **S2** (10.0 mmol) in anhydrous DMSO (0.5 M, 20 mL) was added $Pd(PPh_3)_2Cl_2$ (0.2 mmol), CuI (0.5 mmol), Et_3N (17 mmol) and arylbromide (11 mmol). The mixture was stirred at 90 °C for 2-5 hours. The reaction was cooled to room temperature, water (50 mL) was added, and the mixture was extracted with diethyl ether (50 mL). The combined organic solvent was washed with 10% aqueous HCl (3 × 20 mL), dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The mixture was purified by column chromatography (EtOAc/hexane) to give *alkynone* **1**.

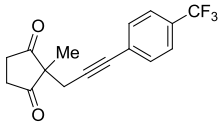
All 2-acetylenic ketones **2** were prepared according to a previously reported procedure.[3]

2-Benzyl-2-(prop-2-yn-1-yl)-1H-indene-1,3(2*H*)-dione (S3):



Prepared according to the general procedure as described above in 95% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a yellow solid; mp = 94 - 96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 5.7, 3.1 Hz, 2H), 7.69 (dd, J = 5.7, 3.1 Hz, 2H), 7.05 – 6.92 (m, 5H), 3.13 (s, 2H), 2.77 (d, J = 2.6 Hz, 2H), 1.75 (t, J = 2.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.5, 142.9, 135.6, 135.2, 131.4, 130.0, 128.3, 128.1, 128.0, 127.0, 123.0, 122.8, 84.1, 84.1, 59.3, 40.1, 25.5; IR (neat): υ_{max} 3324, 2920, 1721, 1591, 1423, 1375, 1209, 1140, 1009, 829, 748 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{14}O_2Na$ $[M+Na]^+$: 297.0886; found: 297.0900.

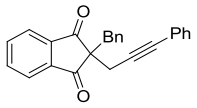
2-Methyl-2-(3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)cyclopentane-1,3-dione (2f):



Prepared according to the general procedure as described above in 84% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a yellow solid; mp = 94 – 96°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 8.2 Hz, 2H), 2.93 – 2.72 (m, 4H), 2.70 (s, 2H), 1.19 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.1, 132.0, 130.2 (q, J_{CF} =

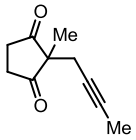
32.7 Hz), 126.5, 125.4 (q, J_{CF} = 3.8 Hz), 123.9 (q, J_{CF} = 272.4 Hz), 86.9, 81.7, 55.5, 35.9, 25.5, 19.4; IR (neat): υ_{max} 3021, 2976, 2833, 1761, 1599, 1523, 1240, 1022, 823, 758 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}F_3O_2$ $[M+H]^+$: 295.0940; found: 295.0978.

2-Benzyl-2-(3-phenylprop-2-yn-1-yl)-1H-indene-1,3(2*H*)-dione (2k):



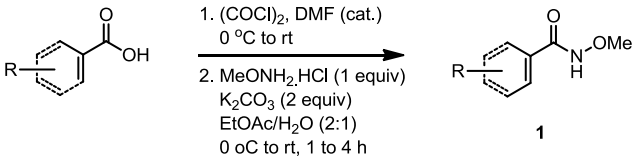
Prepared according to the general procedure as described above in 89% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a yellow solid; mp = 90-92°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (dd, J = 5.7, 3.1 Hz, 2H), 7.62 (dd, J = 5.7, 3.1 Hz, 2H), 7.10 – 7.05 (m, 1H), 7.04 – 6.99 (m, 2H), 6.99 – 6.89 (m, 5H), 6.81 – 6.77 (m, 2H), 3.13 (s, 2H), 2.92 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 142.9, 135.6, 135.3, 131.4, 130.0, 128.3, 128.1, 128.0, 127.0, 123.0, 122.8, 84.1, 84.1, 59.3, 40.1, 25.5; IR (neat): υ_{max} 2925, 1711, 1596, 1441, 1361, 1232, 1104, 1044, 823, 758 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{18}O_2Na$ $[M+Na]^+$: 373.1199; found: 373.1213.

2-(But-2-yn-1-yl)-2-methylcyclopentane-1,3-dione (2t):



Prepared according to the general procedure as described above in 91% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a yellow oil ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.74 (s, 4H), 2.34 (d, J = 4.0, 2.2 Hz, 2H), 1.65 (t, J = 2.2 Hz, 3H), 1.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.8, 78.3, 73.5, 55.5, 35.9, 25.4, 18.7, 3.3; IR (neat): υ_{max} 3014, 2979, 2839, 1766, 1606, 1511, 1248, 1032 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{12}O_2Na$ $[M+H]^+$: 187.0730; found: 187.0734.

IIb. Synthesis of *N*-methoxybenzamide/acrylamide 1



Following same procedure by Guimond and Fagnou *et. al.*[4]

To a stirred solution of the carboxylic acid (10.0 mmol, 1.0 eq.) in dry CH_2Cl_2 (30 mL) at 0 °C under inert atmosphere was added dropwise oxalyl chloride (1.14 mL, 12.0 mmol, 1.2 eq.)

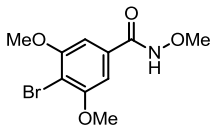
followed by a catalytic amount of dry DMF (2 drops). The reaction was allowed to stir at rt until completion monitored by TLC (~8h). The solvent was then removed under reduce pressure to afford the corresponding crude acid chloride.

Methoxyamine hydrochloride (1.2 equiv.) was added to a biphasic mixture of K_2CO_3 (2.0 equiv.) in a 2:1 mixture of EtOAc and H_2O (0.3 M). The resulting solution was cooled to 0°C followed by dropwise addition of the crude acid chloride dissolved in a minimum amount of EtOAc. The reaction was allowed to stir at room temperature for 8h. The reaction mixture was then diluted with EtOAc, the layers were separated and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The pure products were obtained without any further purification.

N-methoxybenzamides **1a,**[5] **1u,**[6] **1v,**[7] **1w,**[7] **1x,**[8] **1y,**[9] **1z,**[4] **1aa,**[10] **1ab,**[11] **1ae**[4] were prepared according to a previously reported procedure.[4]

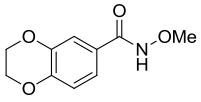
N-methoxyacrylamides **1a1,**[12] **1ao,**[12] **1q**[13] were prepared according to a previously reported procedure.[14]

4-Bromo-N,3,5-trimethoxybenzamide (1ac):



Prepared according to the general procedure as described above in 94% yield from 4-bromo-3,5-dimethoxybenzoic acid and it is a white solid; mp = 201-203 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 (s, 1H), 6.91 (s, 2H), 3.93 (s, 6H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO) δ 164.4, 156.8, 132.2, 104.3, 103.6, 63.8, 56.5; IR (neat): υ_{max} 3154, 2920, 1661, 1576, 1351, 1284, 1012, 914, 858, 767 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{12}BrNO_4Na$ $[M+Na]^+$: 311.9842; found: 311.9857.

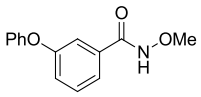
***N*-methoxy-2,3-dihydrobenzo[*b*][1,4]dioxine-6-carboxamide(1ad):**



Prepared according to the general procedure as described above in 96% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a white solid; mp = 168-170 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (br.s, 1H), 7.36 – 7.11 (m, 2H), 6.79 (d, J = 8.4 Hz, 1H),

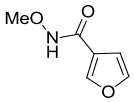
4.20 (s, 4H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 147.0, 143.6, 125.0, 120.6, 117.5, 116.7, 64.8, 64.6, 64.3; IR (neat): υ_{max} 3198, 2938, 1646, 1582, 1493, 1289, 1066, 919, 889, 770 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{11}NO_4Na$ $[M+Na]^+$: 232.0580; found: 232.0590.

***N*-Methoxy-3-phenoxybenzamide(1af) :**



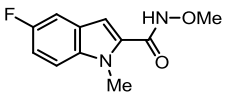
Prepared according to the general procedure as described above in 91% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.68 (br.s, 1H), 7.38 (dd, J = 7.7, 0.8 Hz, 1H), 7.33 (d, J = 1.3 Hz, 1H), 7.23 (t, J = 7.8 Hz, 3H), 7.02 (t, J = 6.4 Hz, 2H), 6.90 (dd, J = 15.1, 5.1 Hz, 2H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 157.1, 156.0, 133.0, 129.5, 129.4, 123.3, 121.5, 121.2, 118.6, 117.0, 63.7; IR (neat): υ_{max} 3179, 2930, 1672, 1579, 1481, 1290, 1062, 920, 888, 767 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{14}NO_3$ $[M+H]^+$: 244.0968 ; found: 244.0981.

***N*-Methoxyfuran-3-carboxamide(1ag) :**



Prepared according to the general procedure as described above in 72% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a white solid; mp = 201-203°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.42 (t, J = 1.5 Hz, 1H), 6.74 (s, 1H), 3.81 (s, 3H).; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 145.5, 143.6, 119.1, 108.6, 64.5; IR (neat): υ_{max} 3126, 2964, 1658, 1521, 1318, 1265, 1062, 914, 842, 756 cm^{-1}; HRMS (ESI) calcd for $C_6H_8NO_3$ $[M+H]^+$: 142.0499; found: 142.0505.

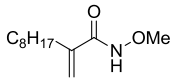
5-Fluoro-*N*-methoxy-1-methyl-1*H*-indole-2-carboxamide (1ah):



Prepared according to the general procedure as described above in 57% yield from 5-fluoro-1-methyl-1*H*-indole-2-carboxylic acid and it is a white solid; mp = 164 – 166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.61 (s, 1H), 7.25 – 7.19 (m, 1H), 7.19 – 7.12 (m, 1H), 7.01 – 6.95 (m, 1H), 6.82 (s, 1H), 3.93 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.1, 158.0 (d, J_{CF}= 236.0 Hz), 135.7, 130.4, 126.0 (d, J_{CF}= 10.4 Hz), 112.9 (d, J_{CF}= 26.7 Hz), 110.9 (d, J_{CF}=

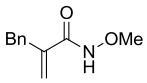
9.5 Hz), 106.1(d, J_{CF}= 23.3 Hz), 104.5, 64.3, 31.6; IR (neat): υ_{max} 3052, 2926, 1658, 1524, 1461, 1225, 1046, 918, 858, 756 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{12}FN_2O_2$ $[M+H]^+$: 223.0877; found: 223.0888

***N*-Bethoxy-2-methylenedecanamide(1ak) :**



Prepared according to the general procedure from corresponding acid[15] as described above in 78% yield. It was purified by flash chromatography (15% EtOAc/hexanes) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.08 (br.s, 1H), 5.55 (s, 1H), 5.26 (s, 1H), 3.76 (s, 3H), 2.26 (t, J = 7.6 Hz, 2H), 1.47 – 1.37 (m, 2H), 1.26-1.22 (m, 10H), 0.85 (t, J = 6.9 Hz, 3H).; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 143.0, 118.3, 64.2, 32.2, 31.8, 29.7, 29.4, 29.2, 27.9, 22.6,14.1; IR (neat): υ_{max} 2923, 2853, 1707, 1649, 1462, 1255, 771 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{24}NO_2[M+H]^+$: 214.1802; found: 214.1813.

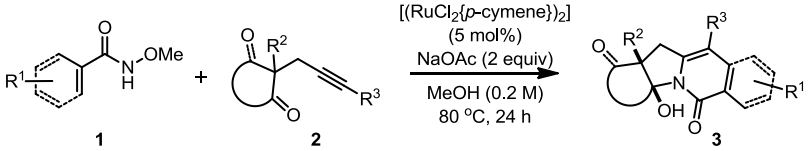
2-Benzyl-*N*-methoxyacrylamide(1am) :



Prepared according to the general procedure from corresponding acid[15] as described above in 81% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.81 (br.s, 1H), 7.15 (t, J = 7.3 Hz, 2H), 7.08 (dd, J = 13.6, 7.2 Hz, 3H), 5.62 (s, 1H), 5.09 (s, 1H), 3.53 (s, 3H), 3.51 (s, 2H) ; ^{13}C NMR (125MHz, $CDCl_3$) δ 166.9, 141.8, 138.0, 129.1, 128.6, 126.6, 120.6, 63.9, 38.3; IR (neat): υ_{max} 2919, 2835, 1716, 1638, 1458, 1249, 834, 773 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{14}NO_2$ $[M+H]^+$: 192.1019; found: 192.1029.

IIc. Ruthenium-catalyzed annulation of 2-acetylenic ketones

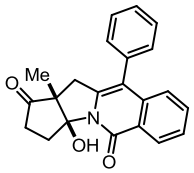
General procedure:



A screw-cap vial equipped with stirred bar was charged with 2-acetylenic ketone **2** (0.4 mmol), *N*-methoxybenzamide/*N*-methoxy acrylamide **1** (0.6 mmol, 1.5 equiv), [$RuCl_2$(*p*-

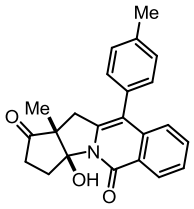
cymene)]$_2$ (18.4 mg, 0.03 mmol, 5.0 mol %) and NaOAc (98.4 mg, 1.2 mmol, 2 equiv) and dry MeOH (2 mL) under nitrogen atmosphere. The reaction mixture was stirred at 80 ^{o}C for 24 hours. Afterwards, it was cooled to room temperature and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (20 to 30% of EtOAc in hexane) to give the desired product **3**.

3a-Hydroxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3a):



Prepared according to the general procedure as described above in 75% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 230 – 232 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (dd, J = 8.0, 1.1 Hz, 1H), 7.57 (ddd, J = 8.3, 7.1, 1.5 Hz, 1H), 7.51 – 7.39 (m, 4H), 7.28-7.26 (m, 1H), 7.26 – 7.20 (m, 2H), 3.41 (ddd, J =13.4, 9.1, 4.0 Hz, 1H), 3.09 (d, J = 17.4 Hz, 1H), 2.80 (d, J = 17.4 Hz, 1H), 2.63 (ddd, J = 18.2, 9.3, 3.8 Hz, 1H), 2.51 (dd, J = 13.4, 11.7, 7.3 Hz, 1H), 2.29 (dt, J = 18.3, 9.3 Hz, 1H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.9, 162.5, 138.4, 138.3, 135.2, 132.9, 130.5, 129.1, 129.0, 128.1, 127.4, 126.3, 125.6, 124.8, 114. 9, 101.5, 56.0, 38.3, 36.5, 31.3, 15.8; IR (neat): υ_{max} 3390, 3189, 2922, 1645, 1576, 1447, 1402, 1112, 772, cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{20}NO_3$ $[M+H]^+$: 346.1438; found: 346.1424.

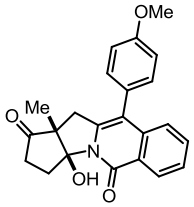
3a-Hydroxy-11a-methyl-10-(*p*-tolyl)-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3b):



Prepared according to the general procedure as described above in 77% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 197 – 199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (dd, J = 8.0, 1.0 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.46 (dt, J = 10.7, 1.8 Hz, 1H), 7.33 – 7.26 (m, 3H), 7.12 (t, J = 8.1 Hz, 2H), 6.73 (s, 1H), 3.46 – 3.39 (m, 1H), 3.09 (d, J = 17.3 Hz, 1H), 2.80 (d, J = 17.4 Hz, 1H), 2.62 (ddd, J = 18.2, 9.3, 3.7 Hz,

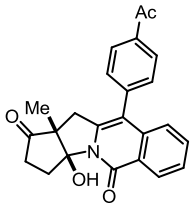
1H), 2.56 – 2.46 (m, 1H), 2.43 (s, 3H), 2.28 (dt, *J* = 18.3, 9.3 Hz, 1H), 1.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.9, 162.5, 138.5, 138.3, 137.8, 132.8, 132.1, 130.4, 129.8, 129.7, 127.3, 126.3, 125.5, 124.9, 116.3, 114.9, 101.5, 56.0, 38.3, 36.5, 31.3, 21.4, 15.8; IR (neat): υ_{max} 3384, 3154, 2926, 1762, 1653, 1532, 1456, 1421, 1154, 884,771 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{21}NO_3Na$ $[M+Na]^+$: 382.1414; found: 382.1404.

3a-Hydroxy-10-(4-methoxyphenyl)-11a-methyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3c):



Prepared according to the general procedure as described above in 78% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 208 – 210 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 1H), 7.46 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.19 – 7.12 (m, 2H), 7.03 – 6.97 (m, 2H), 5.45 (br.s, 1H), 3.87 (s, 3H), 3.46 – 3.38 (m, 1H), 3.09 (d, *J* = 17.3 Hz, 1H), 2.80 (d, *J* = 17.3 Hz, 1H), 2.62 (ddd, *J* = 18.6, 9.4, 3.9 Hz, 1H), 2.51 (dt, *J* = 13.9, 9.6 Hz, 1H), 2.28 (dt, *J* = 18.7, 9.5 Hz, 1H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.0, 162.5, 159.3, 138.6, 138.4, 132.8, 131.6, 127.3, 127.2, 126.3, 125.6, 124.8, 114.5, 101.4, 55.9, 55.5, 38.3, 36.5, 31.3, 15.8; IR (neat): υ_{max} 3169, 2981, 1756, 1647, 1585, 1514, 1324, 1160, 1051, 875, 834, 753 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{21}NO_4Na[M+Na]^+$: 398.1363; found: 398.1369.

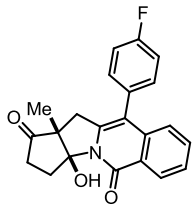
10-(4-Acetylphenyl)-3a-hydroxy-11a-methyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3d):



Prepared according to the general procedure as described above in 45% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp 230 – 232 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (d, *J* = 7.2 Hz, 1H), 8.07 (d, *J* = 8.3 Hz, 2H), 7.58 (t, *J* =

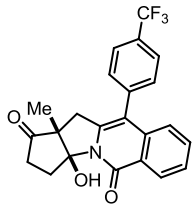
6.9 Hz, 1H), 7.49 (t, *J* = 7.1 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 1H), 3.51 – 3.41 (m, 1H), 3.09 (d, *J* = 17.3 Hz, 1H), 2.80 (d, *J* = 17.3 Hz, 1H), 2.67 (s, 3H), 2.70 – 2.44 (m, 2H), 2.35 – 2.21 (m, 1H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.7, 197.7, 162.4, 140.4, 138.6, 137.7, 136.8, 133.1, 130.9, 129.2, 129.0, 127.6, 126.6, 125.7, 124.4, 113.8, 101.5, 56.0, 38.2, 36.4, 31.2, 26.8, 15.8; IR (neat): υ_{max} 3340, 3041, 2958, 1756, 1640, 1219, 1041, 819, 772 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{21}NO_4Na[M+Na]^+$: 410.1363; found: 410.1369.

10-(4-Fluorophenyl)-3a-hydroxy-11a-methyl-3,3a,11,11a-tetrahydro-1H-cyclopenta[4,5]pyrrolo[1,2-b]isoquinoline-1,5(2H)-dione (3e):



Prepared according to the general procedure as described above in 72% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 210 – 212 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.0 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.26 – 7.12 (m, 5H), 5.55 (br.s, 1H), 3.48 (ddd, *J* = 13.1, 9.4, 3.8 Hz, 1H), 3.07 (d, *J* = 17.2 Hz, 1H), 2.79 (d, *J* = 17.3 Hz, 1H), 2.62 (ddd, *J* = 18.7, 9.4, 3.6 Hz, 1H), 2.51 (dt, *J* = 13.9, 9.7 Hz, 1H), 2.26 (dt, *J* = 19.0, 9.7 Hz, 1H), 1.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.9, 162.6 (d, J_{CF} = 247.7 Hz), 162.4, 138.7, 138.3, 133.0, 132.2 (dd, J_{CF} = 6.8, 6.8 Hz), 131.1 (d, J_{CF}= 2.6 Hz), 127.4, 126.4, 125.6, 124.5, 116.1 (dd, J_{CF} = 21.3, 11.8 Hz), 113.8, 101.5, 56.0, 38.2, 36.4, 31.0, 15.80; IR (neat): υ_{max} 3310, 2936, 1745, 1651, 1510, 1220, 908, 771 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{19}FNO_3[M+H]^+$: 364.1343; found: 364.1345.

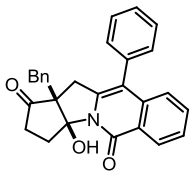
3a-Hydroxy-11a-methyl-10-(4-(trifluoromethyl)phenyl)-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3f):



Prepared according to the general procedure as described above in 41% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 226 – 228 °C;

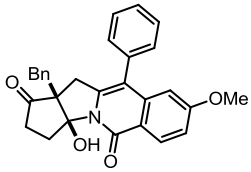
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (dd, J = 8.0, 1.0 Hz, 1H), 7.75 (t, J = 6.9 Hz, 2H), 7.58 (ddd, J = 8.3, 7.1, 1.4 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.40 (dd, J = 15.7, 7.9 Hz, 2H), 7.18 (d, J = 8.0 Hz, 1H), 5.32 (s, 1H), 3.51 – 3.45 (m, 1H), 3.07 (d, J = 17.2 Hz, 1H), 2.79 (d, J = 17.2 Hz, 1H), 2.64 (ddd, J = 18.8, 9.5, 3.6 Hz, 1H), 2.51 (dt, J = 14.0, 9.8 Hz, 1H), 2.32 – 2.23 (m, 1H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.7, 162.4, 139.1, 138.8, 137.7, 133.1, 131.1, 130.4 (q, J_{CF} = 27.3 Hz), 127.6, 126.6, 126.1 (q, J_{CF} = 2.6 Hz), 125.7, 124.4, 113.4, 101.5, 56.0, 38.2, 36.3, 31.0, 15.8; IR (neat): υ_{max} 3341, 2943, 1746, 1653, 1324, 1166, 1126, 1068, 853, 769 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}F_3NO_3$ $[M+H]^+$: 414.1312; found: 414.1300.

11a-Benzyl-3a-hydroxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3g):



Prepared according to the general procedure as described above in 70% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 220 – 222°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, J = 7.9 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.43 – 7.32 (m, 4H), 7.21 (dd, J = 7.6, 1.6 Hz, 2H), 7.18 – 7.10 (m, 5H), 7.02 (d, J = 7.2 Hz, 1H), 5.53 (br.s, 1H), 3.25 – 3.18 (m, 1H), 3.04 (d, J = 17.1 Hz, 1H), 3.04 (s, 2H), 2.85 (d, J = 17.1 Hz, 1H), 2.16 – 2.02 (m, 2H), 1.94 (dt, J = 13.7, 10.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.4, 162.3, 138.2, 138.0, 135.8, 135.1, 132.8, 131.0, 130.6, 129.1, 128.9, 128.3, 128.0, 127.3, 127.1, 126.2, 125.6, 124.8, 114.7, 101.6, 61.1, 37.3, 37.0, 36.7, 31.4; IR (neat): υ_{max} 3473, 2971, 1743, 1650, 1621, 1596, 1527, 1336, 816, 771, 727 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{24}NO_3$ $[M+H]^+$: 422.1751 ; found: 422.1752.

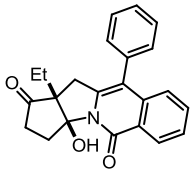
11a-Benzyl-3a-hydroxy-8-methoxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3h):



Prepared according to the general procedure as described above in 81% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 202 – 204 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 6.8 Hz, 1H), 7.38 (dd, J = 16.3, 7.9 Hz, 2H), 7.35

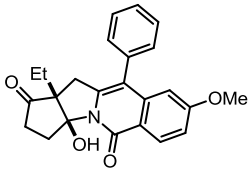
– 7.30 (m, 1H), 7.26 – 7.19 (m, 2H), 7.18 – 7.09 (m, 4H), 7.02 (d, *J* = 7.0 Hz, 1H), 6.94 (d, *J* = 6.4 Hz, 1H), 6.47 (s, 1H), 5.81 (br.s, 1H), 3.63 (s, 3H), 3.32 – 3.30 (m, 1H), 3.03 (s, 2H), 3.01 (d, *J* = 17.1 Hz, 1H), 2.82 (d, *J* = 17.1 Hz, 1H), 2.15 – 2.00 (m, 2H), 1.92 (dd, *J* = 22.2, 10.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.5, 163.2, 140.5, 138.8, 135.9, 135.2, 131.0, 130.5, 129.3, 129.1, 128.9, 128.2, 128.0, 127.0, 119.7, 115.3, 114.4, 106.4, 101.4, 61.1, 55.5, 37.4, 37.0, 36.7, 31.5; IR (neat): υ_{max} 3313, 2916, 1742, 1649, 1598, 1485, 1275, 1229, 1034, 855, 762, 703 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{26}NO_4$ $[M+H]^+$: 452.1856; found: 452.1885.

11a-Ethyl-3a-hydroxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3i):



Prepared according to the general procedure as described above in 72% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 198 – 200 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.0 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.46 – 7.33 (m, 4H), 7.22 – 7.13 (m, 3H), 5.18 (br.s, 1H), 3.46 – 3.39 (m, 1H), 3.01 (d, *J* = 17.3 Hz, 1H), 2.74 (d, *J* = 17.3 Hz, 1H), 2.54 (ddd, *J* = 18.7, 9.9, 3.5 Hz, 1H), 2.44 (dt, *J* = 14.0, 9.8 Hz, 1H), 2.19 (dt, *J* = 18.9, 9.6 Hz, 1H), 1.79 (dq, *J* = 15.0, 7.5 Hz, 1H), 1.70 (dq, *J* = 14.7, 7.4 Hz, 1H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.1, 162.3, 138.6, 138.4, 135.3, 132.8, 130.6, 130.5, 129.2, 129.0, 128.0, 127.3, 126.3, 125.6, 124.8, 114.6, 101.7, 59.4, 36.8, 31.9, 24.1, 9.0; IR (neat): υmax 3316, 2984, 1752,1651, 1565, 1402,1361,1265, 1044, 825, 772 cm^{-1};HRMS (ESI) calcd for $C_{23}H_{22}NO_3$ $[M+H]^+$: 360.1594; found: 360.1595.

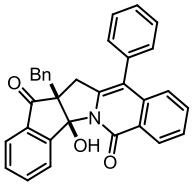
11a-Ethyl-3a-hydroxy-8-methoxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3j):



Prepared according to the general procedure as described above in 84% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 180 – 182 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.8 Hz, 1H), 7.47 (dd, *J* = 16.0, 7.7 Hz, 2H), 7.42 (dd, *J* = 16.6, 9.2 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.03 (dd, *J* =

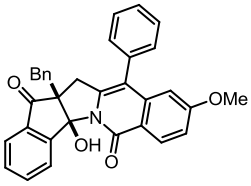
8.6, 2.1 Hz, 1H), 6.58 (d, *J* = 2.4 Hz, 1H), 3.72 (s, 3H), 3.50 (ddd, *J* = 12.8, 9.4, 3.1 Hz, 1H), 3.04 (d, *J* = 17.3 Hz, 1H), 2.78 (d, *J* = 17.3 Hz, 1H), 2.60 (ddd, *J* = 18.7, 9.8, 2.8 Hz, 1H), 2.49 (dt, *J* = 13.7, 9.9 Hz, 1H), 2.25 (dt, *J* = 18.8, 9.5 Hz, 1H), 1.85 (dq, *J* = 15.0, 7.5 Hz, 1H), 1.76 (dq, *J* = 14.6, 7.4 Hz, 1H), 0.95 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.3, 163.3, 140.6, 139.4, 135.4, 130.6, 130.4, 129.4, 129.2, 129.0, 128.0, 119.6, 115.3, 114.3, 106.4, 101.6, 59.4, 55.5, 36.9, 36.8, 31.9, 24.1, 9.0; IR (neat): υ_{max} 3314, 2916, 1762, 1641, 1599, 1465, 1325, 1223, 1046, 818, 772 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{23}NO_4Na$ $[M+Na]^+$: 412.1519; found: 412.1541.

12a-Benzyl-4b-hydroxy-11-phenyl-12,12a-dihydro-4b*H*-indeno[2',1':4,5]pyrrolo[1,2-*b*]isoquinoline-6,13-dione (3k):



Prepared according to the general procedure as described above in 62% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 181 – 183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 – 8.34 (m, 2H), 7.68 – 7.59 (m, 2H), 7.48 – 7.36 (m, 3H), 7.36 – 7.27 (m, 3H), 7.21 – 7.16 (m, 2H), 7.05 (d, *J* = 7.9 Hz, 1H), 7.03 – 6.94 (m, 4H), 6.77 (s, 1H), 6.72 – 6.66 (m, 1H), 3.34 (d, *J* = 14.0 Hz, 1H), 3.15 (d, *J* = 13.9 Hz, 1H), 2.94 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 162.7, 151.7, 138.3, 138.1, 136.2, 136.0, 134.7, 134.3, 132.8, 131.0, 130.8, 130.6, 130.3, 128.9, 128.8, 128.0, 127.2, 126.7, 126.5, 126.3, 125.1, 124.77, 123.9, 114.9, 100.3, 77.5, 77.2, 76.8, 62.0, 35.7, 35.6; IR (neat): υ_{max} 3327, 2934, 1750, 1656, 1641, 1425, 1365, 1241, 1065, 872, 772 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{23}NO_3Na$ $[M+Na]^+$: 492.1570; found: 492.1596.

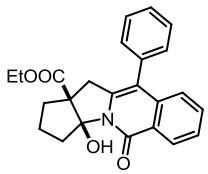
12a-Benzyl-4b-hydroxy-9-methoxy-11-phenyl-12,12a-dihydro-4b*H*-indeno[2',1':4,5]pyrrolo[1,2-*b*]isoquinoline-6,13-dione (3l):



Prepared according to the general procedure as described above in 78% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp = 130 – 132°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, *J* = 9.0 Hz, 1H), 8.36 (d, *J* = 9.0 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.47 (dd, *J* = 12.9, 5.5 Hz, 1H), 7.42 – 7.33 (m, 3H), 7.29 – 7.23 (m, 2H), 7.13 –

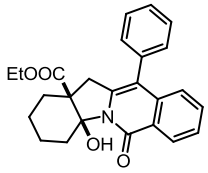
7.05 (m, 4H), 7.01 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.97 (br.s, 1H), 6.77 – 6.73 (m, 1H), 6.45 (d, *J* = 2.4 Hz, 1H), 3.67 (s, 3H), 3.41 (d, *J* = 14.0 Hz, 1H), 3.21 (d, *J* = 14.0 Hz, 1H), 2.97 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.0, 163.3, 162.3, 151.8, 140.6, 138.8, 136.3, 136.0, 134.8, 134.2, 131.0, 130.7, 130.5, 130.3, 129.3, 129.0, 128.8, 128.0, 126.6, 126.6, 123.8, 118.9, 115.3, 114.5, 106.3, 100.2, 62.0, 55.4, 35.7, 35.6; IR (neat): υ_{max} 3329, 2939, 1757, 1661, 1643,1432, 1239, 1054, 996, 869, 773 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{26}NO_4$ $[M+H]^+$: 500.1856; found: 500.1876.

Ethyl 3a-hydroxy-5-oxo-10-phenyl-2,3,3a,5,11,11a-hexahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-11a-carboxylate (3m):



Prepared according to the general procedure as described above in 73% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp 162 – 164 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 1H), 7.52 – 7.40 (m, 4H), 7.38 – 7.34 (m, 1H), 7.31 (d, *J* = 7.4 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 5.64 (s, 1H), 4.26 – 4.15 (m, 2H), 3.71 (d, *J* = 17.7 Hz, 1H), 2.84 – 2.77 (m, 1H), 2.72 – 2.66 (m, 1H), 2.67 (d, *J* = 17.7 Hz, 1H), 2.45 – 2.37 (m, 1H), 2.10 – 2.01 (m, 1H), 1.73 – 1.59 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 161.9, 139.8, 138.6, 135.6, 132.6, 130.8, 130.6, 129.2, 128.9, 127.9, 127.3, 125.9, 125.4, 124.6, 113.7, 107.3, 61.6, 59.8, 40.3, 38.9, 35.9, 24.2, 14.3; IR (neat): υ_{max} 3335, 2959, 1729, 1657, 1624, 1507, 1444, 1280, 1184, 1106, 1026, 890, 759 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{23}NO_4Na$ $[M+Na]^+$: 412.1519; found: 412.1523.

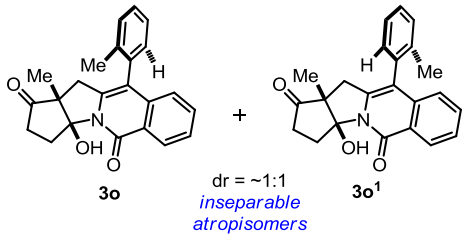
Ethyl 4a-hydroxy-6-oxo-11-phenyl-1,2,3,4,4a,6,12,12a-octahydroindolo[1,2-*b*] isoquinoline-12a-carboxylate (3n):



Prepared according to the general procedure as described above in 76% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid ; mp = 170 – 172°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, *J* = 8.1, 1.0 Hz, 1H), 7.60 – 7.39 (m, 5H), 7.39 – 7.27 (m, 3H), 5.83 (s, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.08 (d, *J* = 16.6 Hz, 1H), 2.79 (d, *J* = 16.6

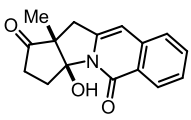
Hz, 1H), 2.66 (ddd, *J* = 14.0, 6.0, 3.2 Hz, 1H), 2.34 (ddd, *J* = 14.5, 10.3, 4.1 Hz, 2H), 1.83 – 1.48 (m, 4H), 1.47 – 1.30 (m, 1H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 162.5, 139.0, 138.1, 135.7, 132.5, 130.7, 129.1, 128.9, 127.9, 127.3, 126.0, 125.6, 124.5, 114.7, 96.2, 61.3, 53.7, 35.4, 35.1, 29.1, 21.2, 21.2, 14.2; IR (neat): υ_{max} 3345, 2962, 1733, 1648, 1634, 1587, 1456, 1325,1365, 1196, 1052, 995, 859, 775 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{26}NO_4$ $[M+H]^+$: 404.1856; found: 404.1826.

3a-Hydroxy-11a-methyl-10-(*o*-tolyl)-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3o & 3o[1]; mixture of atropisomers:



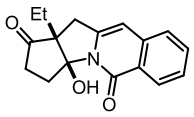
Prepared according to the general procedure as described above in 76% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 191 – 193 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.49 – 7.44 (m, 1H), 7.38 – 7.31 (m, 2H), 7.30 – 7.26 (m, 1H), 7.11 – 7.08 (m, 1H), 7.00 (dd, *J* = 7.8, 4.6 Hz, 1H), 3.51 – 3.44 (m, 0.5H), 3.33 (ddd, *J* = 13.9, 9.2, 4.5 Hz, 0.5H), 3.01 (d, *J* = 17.3 Hz, 0.5H), 2.83 (d, *J* = 17.3 Hz, 0.5H), 2.74 (d, *J* = 17.3 Hz, 0.5H), 2.69 – 2.59 (m, 1H), 2.59 – 2.51 (m, 1H), 2.51 – 2.44 (m, 0.5H), 2.32 (dt, *J* = 18.1, 9.0 Hz, 0.5H), 2.21 (ddd, *J* = 12.1, 10.7, 5.6 Hz, 0.5H), 2.00 (s, 1.5H), 1.98 (s, 1.5H), 1.24 (s, 1.5H), 1.24 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.0, 217.6, 162.6, 138.4, 138.2, 138.1, 137.7, 137.5, 134.5, 134.3, 133.0, 130.9, 130.8, 130.7, 130.6, 128.6, 127.4, 126.7, 126.5, 126.4, 125.7, 125.5, 124.6, 114.2, 113.7, 101.4, 101.3, 56.0, 38.3, 38.0, 36.6, 36.5, 31.6, 31.0, 19.8, 19.6, 15.8, 15.7; IR (neat): υ_{max} 3384, 3154, 2936, 1752, 1653, 1532, 1456, 1421, 1325, 1154, 1065, 884, 771 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{21}NO_3Na$ $[M+Na]^+$: 382.1414; found: 287.1427.

3a-Hydroxy-11a-methyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-b]isoquinoline-1,5(2*H*)-dione (3p):



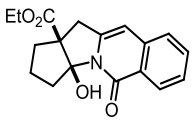
Prepared according to the general procedure as described above in 80% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 154 – 156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (dd, J = 4.6, 3.9 Hz, 1H), 7.63 (ddd, J = 8.2, 5.6, 1.4 Hz, 1H), 7.49 – 7.40 (m, 2H), 6.34 (s, 1H), 5.37 (br.s, 1H), 3.38 (ddd, J = 13.4, 8.9, 3.7 Hz, 1H), 3.24 (dd, J = 16.9, 1.1 Hz, 1H), 2.97 (dd, J = 16.9, 1.7 Hz, 1H), 2.60 (ddd, J = 18.5, 9.3, 3.7 Hz, 1H), 2.52 – 2.43 (m, 1H), 2.26 – 2.15 (m, 1H), 1.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.0, 162.8, 140.9, 138.3, 133.0, 127.3, 126.3, 126.0, 125.5, 101.5, 100.9, 56.2, 38.4, 36.5, 31.1, 15.8; IR (neat): υ_{max} 3341, 2953, 1744, 1660, 1625, 1598, 1456, 1339, 1141, 1074, 820, 757 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NO_3$ $[M+H]^+$: 270.1125 ; found: 270.1136.

11a-Ethyl-3a-hydroxy-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3q):



Prepared according to the general procedure as described above in 78% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 170 – 172 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 6.33 (s, 1H), 5.20 (br.s, 1H), 3.58 – 3.38 (m, 1H), 3.25 (d, J = 16.8 Hz, 1H), 3.00 (d, J = 16.8 Hz, 1H), 2.64 – 2.39 (m, 2H), 2.23 – 2.09 (m, 1H), 1.86 (tdd, J = 21.4, 14.3, 7.4 Hz, 2H), 1.02 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.2, 162.8, 141.2, 138.3, 132.9, 127.3, 126.3, 126.0, 125.5, 101.3, 101.1, 59.6, 37.1, 36.8, 31.6, 24.1, 9.0; IR (neat): υ_{max} 3326, 2925, 1762, 1654, 1632, 1575, 1424, 1356, 12685, 1044, 825, 772cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{18}NO_3$ $[M+H]^+$: 284.1281; found: 284.1252.

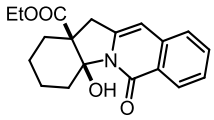
Ethyl 3a-hydroxy-5-oxo-2,3,3a,5,11,11a-hexahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-11a-carboxylate (3r):



Prepared according to the general procedure as described above in 75% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.1 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 6.39 (s, 1H), 4.23 (dq, J = 14.2, 1.9 Hz, 2H), 3.93 (d, J = 17.4 Hz, 1H), 2.88 (d, J = 17.5 Hz, 1H), 2.80 – 2.68 (m, 2H), 2.37 (ddd, J = 13.6, 10.3, 7.5 Hz, 1H), 2.03 (dddd,

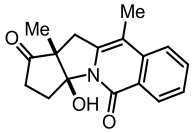
J = 14.8, 11.1, 7.4, 3.8 Hz, 1H), 1.80 – 1.72 (m, 1H), 1.58 (dddd, *J* = 17.0, 13.7, 10.0, 7.0 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 162.4, 142.3, 138.7, 132.7, 127.2, 125.9, 125.8, 125.3, 106.9, 100.4, 61.7, 59.8, 40.1, 39.0, 36.3, 24.2, 14.3; IR (neat): υmax 3360, 2938, 1731, 1650, 1620, 1595, 1443, 1327, 1189, 1110, 1031, 772, 702 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{19}NO_4Na$ $[M+Na]^+$: 336.1206 ; found: 336.1229.

Ethyl 4a-hydroxy-6-oxo-1,2,3,4,4a,6,12,12a-octahydroindolo[1,2-*b*]isoquinoline-12a-carboxylate (3s):



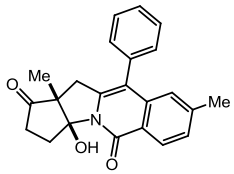
Prepared according to the general procedure as described above 72% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a colorless oil; ^{1}H NMR (300 MHz, CDCl3) δ 8.34 (d, *J* = 8.1 Hz, 1H), 7.62 (t, *J* = 7.0 Hz, 1H), 7.51 – 7.39 (m, 2H), 6.45 (s, 1H), 4.22 – 4.07 (m, 2H), 3.30 (d, *J* = 16.3 Hz, 1H), 2.95 (d, *J* = 16.1 Hz, 1H), 2.64 – 2.53 (m, 1H), 2.37 (ddd, *J* = 18.7, 14.4, 7.1 Hz, 2H), 1.86 – 1.56 (m, 4H), 1.54-1.36 (m, 1H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 163.1, 141.5, 138.3, 132.8, 132.6, 127.3, 126.0, 125.7, 101.6, 95.8, 61.3, 53.8, 36.1, 34.8, 29.8, 29.6, 21.3, 14.1; IR (neat): υmax 3473, 2970, 2839, 1766, 1687, 1606, 1511, 1248, 1165, 1032, 834, 773 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{22}NO_4$ $[M+H]^+$: 328.1543 ; found: 328.1561.

3a-Hydroxy-10,11a-dimethyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3t):



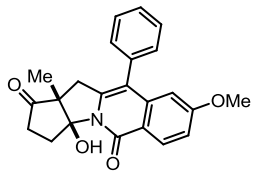
Prepared according to the general procedure as described above in 80% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a white solid ; mp = 210 – 212 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.0 Hz, 1H), 7.74 – 7.67 (m, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 5.39 (s, 1H), 3.36 (ddd, *J* = 12.7, 8.9, 3.8 Hz, 1H), 3.30 (d, *J* = 17.0 Hz, 1H), 2.94 (d, *J* = 17.0 Hz, 1H), 2.67 – 2.41 (m, 2H), 2.29 – 2.15 (m, 1H), 2.19 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.3, 162.4, 138.5, 137.1, 132.9, 127.6, 126.1, 125.7, 122.9, 106.9, 101.2, 55.8, 38.0, 36.5, 31.3, 16.0, 13.1; IR (neat): υmax 3482, 2979, 1750, 1642, 1621, 1462, 1358, 1126, 1043, 820, 773 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{18}NO_3$ $[M+H]^+$: 284.1281; found: 287.1301.

3a-Hydroxy-8,11a-dimethyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3u) :



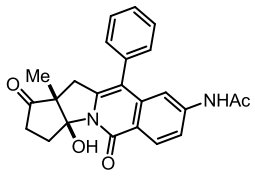
Prepared according to the general procedure as described above in 82% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp = 172 – 174 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, J = 8.2 Hz, 1H), 7.45 – 7.31 (m, 3H), 7.20 (d, J = 2.9 Hz, 1H), 7.14 (d, J = 8.7 Hz, 2H), 6.93 (s, 1H), 3.51 – 3.37 (m, 1H), 2.99 (d, J = 17.3 Hz, 1H), 2.71 (d, J = 17.3 Hz, 1H), 2.52 (ddd, J = 15.5, 7.6, 3.9 Hz, 1H), 2.45 – 2.33 (m, 1H), 2.27 (s, 3H), 2.19 (dd, J = 18.0, 9.7 Hz, 1H), 1.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.1, 162.2, 143.4, 138.4, 138.2, 135.2, 130.7, 128.9, 128.8, 127.8, 127.9, 124.2, 123.2, 114.5, 101.2, 55.9, 38.0, 36.3, 30.8, 22.0, 15.6.; IR (neat): υ_{max} 3364, 3154, 2926, 1732, 1673, 1532, 1456, 1421, 1154, 884, 771 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{22}NO_3$ $[M+H]^+$: 360.1594; found: 360.1610.

3a-Hydroxy-8-methoxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3v)



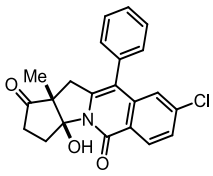
Prepared according to the general procedure as described above in 81% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 212 – 214 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 8.9 Hz, 1H), 7.52 – 7.37 (m, 3H), 7.22 (d, J = 6.9 Hz, 2H), 7.02 (dd, J = 8.8, 2.1 Hz, 1H), 6.59 (d, J = 2.2 Hz, 1H), 3.71 (s, 3H), 3.47 (dd, J = 16.2, 6.5 Hz, 1H), 3.06 (d, J = 17.3 Hz, 1H), 2.78 (d, J = 17.4 Hz, 1H), 2.67 – 2.42 (m, 2H), 2.35 – 2.19 (m, 1H), 1.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.1, 163.2, 140.4, 139.1, 135.2, 130.4, 130.3, 129.4, 129.1, 128.9, 127.9, 119.4, 115.2, 114.4, 106.3, 101.2, 55.9, 55.4, 38.2, 36.3, 31.0, 15.7; IR (neat): υ_{max} 3369, 2961, 1768, 1647, 1575, 1514, 1324, 1160, 1051, 875, 834, 753 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{22}NO_4$ $[M+H]^+$: 376.1543 ; found: 376.1523.

***N*-(3a-Hydroxy-11a-methyl-1,5-dioxo-10-phenyl-2,3,3a,5,11,11a-hexahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinolin-8-yl)acetamide (3w) :**



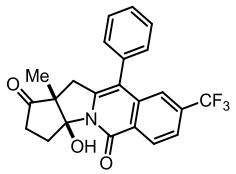
Prepared according to the general procedure as described above in 78% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 240 – 242 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, J = 8.7 Hz, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.30 – 7.45 (m, 4H), 7.14 (d, J = 5.9 Hz, 3H), 5.36 (br.s, 1H), 3.44 – 3.30 (m, 1H), 2.99 (d, J = 17.4 Hz, 1H), 2.71 (d, J = 17.4 Hz, 1H), 2.61 – 2.34 (m, 2H), 2.29 – 2.09 (m, 1H), 2.04 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.8, 168.5, 161.7, 142.0, 139.3, 139.0, 134.9, 130.3, 129.0, 128.7, 128.0, 121.6, 118.3, 114.3, 113.2, 101.2, 55.8, 38.1, 36.3, 31.1, 24.7, 15.7; IR (neat): υ_{max} 3401, 2881, 2724, 1743, 1650, 1634, 1534, 1485, 1219, 1035, 771, 732 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{23}N_2O_4$ $[M+H]^+$: 403.1652; found: 403.1667.

8-Chloro-3a-hydroxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3x):



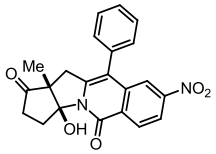
Prepared according to the general procedure as described above in 76% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp = 160 – 162 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (d, J = 8.6 Hz, 1H), 7.54 – 7.42 (m, 3H), 7.40 (dd, J = 8.6, 1.9 Hz, 1H), 7.23 – 7.19 (m, 3H), 3.51 – 3.37 (m, 1H), 3.08 (d, J = 17.5 Hz, 1H), 2.79 (d, J = 17.5 Hz, 1H), 2.63 (ddd, J = 17.7, 9.2, 3.3 Hz, 1H), 2.52 (ddd, J = 23.0, 13.1, 6.2 Hz, 1H), 2.36 – 2.18 (m, 1H), 1.24 (s, 3H).; ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.6, 161.8, 140.0, 139.7, 134.5, 130.4, 129.4, 129.2, 129.2, 128.9, 126.9, 124.2, 124.0, 114.0, 101.6, 55.9, 38.4, 36.4, 31.8, 15.8.; IR (neat): υ_{max} 3348, 2961, 1746, 1699, 1653, 1468, 1520, 1219, 1136, 1042, 772 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{19}ClNO_3$ $[M+H]^+$: 380.1048 ; found: 380.1055.

3a-Hydroxy-11a-methyl-10-phenyl-8-(trifluoromethyl)-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3y):



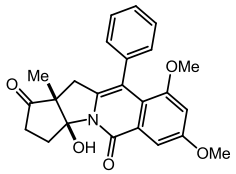
Prepared according to the general procedure as described above in 46% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, J = 8.4 Hz, 1H), 7.57 (dd, J = 8.4, 1.3 Hz, 1H), 7.47 – 7.36 (m, 4H), 7.18 – 7.12 (m, 2H), 3.43 (ddd, J = 13.1, 9.7, 5.1 Hz, 1H), 3.08 – 3.03 (m, 1H), 2.76 (d, J = 17.5 Hz, 1H), 2.57 (ddd, J = 18.8, 9.5, 3.6 Hz, 1H), 2.49 – 2.41 (m, 1H), 2.20 (dt, J = 19.0, 9.5 Hz, 1H), 1.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.4, 161.4, 140.2, 138.3, 134.5, 134.1, 130.2, 129.3, 129.2, 128.4, 127.6, 122.2, 121.9, 114.5, 101.7, 55.9, 38.2, 36.2, 30.7, 15.7, 14.8; IR (neat): υ_{max} 3314, 2961, 1743, 1656, 1436, 1316, 1235, 1130, 1075, 848, 772, 704 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{18}F_3NO_3Na$ $[M+Na]^+$: 436.1131 ; found: 436.1108.

3a-Hydroxy-11a-methyl-8-nitro-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3z):



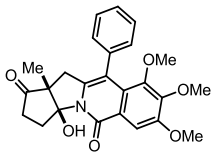
Prepared according to the general procedure as described above in 61% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp = 215 – 217 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, J = 8.8 Hz, 1H), 8.18 (dd, J = 8.8, 2.1 Hz, 1H), 8.09 (d, J = 2.0 Hz, 1H), 7.63 – 7.43 (m, 3H), 7.25 – 7.21 (m, 2H), 5.34 (br.s, 1H), 3.55 – 3.35 (m, 1H), 3.15 (d, J = 17.6 Hz, 1H), 2.85 (t, J = 15.6 Hz, 1H), 2.66 (ddd, J = 18.9, 9.6, 3.7 Hz, 1H), 2.53 (dt, J = 14.0, 9.8 Hz, 1H), 2.29 (dt, J = 19.0, 9.6 Hz, 1H), 1.26 (s, 3H).; ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.1, 161.1, 150.7, 141.3, 139.1, 133.7, 130.3, 129.6, 129.5, 129.1, 128.8, 120.3, 119.9, 114.8, 101.9, 56.0, 38.4, 36.3, 30.9, 15.8; IR (neat): υ_{max} 3316, 2961, 1746, 1656, 1617, 1527, 1425, 1344, 1219, 1035, 996, 862, 770 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{19}N_2O_5$ $[M+H]^+$: 391.1288; found: 391.1267.

3a-Hydroxy-7,9-dimethoxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3aa) :



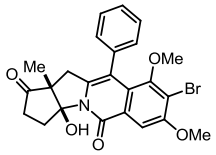
Prepared according to the general procedure as described above in 83% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 187 – 189 °C; ^{1}H NMR (500 MHz, $CDCl_3$); δ 7.49 (d, J = 2.5 Hz, 1H), 7.38 – 7.26 (m, 3H), 7.17 (d, J = 7.5 Hz, 1H), 7.08 (d, J = 7.2 Hz, 1H), 6.61 (d, J = 2.5 Hz, 1H), 5.81 (br.s, 1H), 3.92 (s, 3H), 3.46 – 3.39 (m, 1H), 3.33 (s, 3H), 2.97 (d, J = 17.3 Hz, 1H), 2.67 – 2.56 (m, 2H), 2.49 (dt, J = 13.8, 9.6 Hz, 1H), 2.27 (dt, J = 15.4, 9.5 Hz, 1H), 1.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.8, 161.4, 158.9, 157.2, 139.4, 136.1, 129.1, 129.1, 128.0, 127.7, 127.4, 126.4, 123.1, 113.2, 105.7, 101.5, 99.0, 55.6, 55.5, 38.3, 36.3, 31.0, 15.6.;IR (neat): υ_{max} 3384, 3054, 2936, 1782, 1653, 1582, 1535, 1421, 1194, 1065, 994, 835, 771, cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{24}NO_5$ $[M+H]^+$: 406.1649; found: 406.1638.

3a-Hydroxy-7,8,9-trimethoxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3ab):



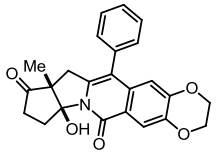
Prepared according to the general procedure as described above in 89% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 238 – 240 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.45 – 7.32 (m, 3H), 7.25 (d, J = 7.1 Hz, 1H), 7.17 (d, J = 7.2 Hz, 1H), 4.02 (s, 3H), 3.88 (s, 3H), 3.49 – 3.35 (m, 1H), 3.18 (s, 3H), 2.99 – 2.87 (m, 1H), 2.61 (dq, J = 9.2, 6.5 Hz, 2H), 2.50 (dd, J = 9.3, 4.2 Hz, 1H), 2.30 (dd, J = 18.0, 9.5 Hz, 1H), 1.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.5, 161.1, 152.4, 149.1, 147.8, 138.4, 137.0, 129.0, 127.7, 127.5, 127.1, 126.4, 121.9, 112.4, 103.4, 101.2, 60.6, 60.4, 55.8, 55.3, 38.1, 36.0, 30.9, 15.3; IR (neat): υ_{max} 3384, 3164, 2986, 1742, 1653, 1562, 1486, 1421, 1154, 1098, 854, 784,771, cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{25}NO_6Na$ $[M+Na]^+$: 458.1574 ; found: 458.1562.

8-Bromo-3a-hydroxy-7,9-dimethoxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3ac):



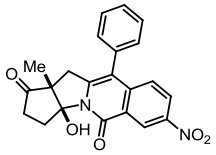
Prepared according to the general procedure as described above in 86% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 241 – 243 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.35 – 7.24 (m, 3H), 7.20 (t, J = 2.0 Hz, 1H), 7.12 (dd, J = 5.1, 3.5 Hz, 1H), 5.44 (br.s, 1H), 3.96 (s, 3H), 3.39 – 3.23 (m, 1H), 3.01 (d, J = 3.5 Hz, 3H), 2.91 (d, J = 17.5 Hz, 1H), 2.60 – 2.52 (m, 2H), 2.43 (dt, J = 13.9, 9.6 Hz, 1H), 2.22 (dt, J = 18.9, 9.5 Hz, 1H), 1.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.5, 161.3, 155.3, 154.8, 138.1, 137.7, 129.9, 129.7, 128.0, 127.9, 127.1, 126.8, 116.0, 112.2, 103.7, 101.7, 60.9, 56.7, 55.6, 38.6, 36.3, 31.1, 15.6; IR (neat): υ_{max} 3361, 2929, 1746, 1642, 1585, 1461, 1356, 1208, 1167, 1094, 862, 755 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{23}BrNO_5$ $[M+H]^+$: 484.0754 ; found: 484.0757.

7a-Hydroxy-10a-methyl-12-phenyl-8,9,10a,11-tetrahydro-2*H*-cyclopenta[4,5]pyrrolo[1,2-*b*][1,4]dioxino[2,3-*g*]isoquinoline-6,10(3*H*,7a*H*)-dione (3ad):



Prepared according to the general procedure as described above in 78% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 228 – 230 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.8 Hz, 1H), 7.37 – 7.27 (m, 3H), 7.19 (d, J = 7.4 Hz, 1H), 7.12 (dd, J = 5.1, 3.4 Hz, 1H), 7.00 (d, J = 8.8 Hz, 1H), 5.42 (br.s, 1H), 4.17 – 4.13 (m, 2H), 3.79 – 3.75 (m, 2H), 3.36 (ddd, J = 13.5, 9.2, 3.9 Hz, 1H), 2.96 (d, J = 17.5 Hz, 1H), 2.64 – 2.56 (m, 2H), 2.47 (dt, J = 13.8, 9.6 Hz, 1H), 2.27 (dt, J = 18.9, 9.5 Hz, 1H), 1.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.0, 161.9, 146.9, 139.3, 138.4, 129.6, 129.5, 128.7, 127.9, 127.7, 126.7, 120.8, 120.5, 117.3, 112.4, 101.5, 64.3, 63.2, 55.7, 38.7, 36.5, 31.5, 15.7; IR (neat): υ_{max} 3316, 2926, 1745, 1643, 1592, 1467, 1344, 1282, 1064, 865, 775 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{22}NO_5$ $[M+H]^+$: 404.1492 ; found: 404.1472.

3a-Hydroxy-11a-methyl-7-nitro-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3ae) :

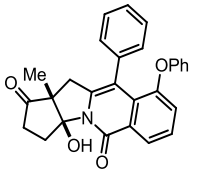


Prepared according to the general procedure as described above in 65% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a yellow solid; mp = 236 – 238 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.19 (d, J = 2.4 Hz, 1H), 8.23 (dd, J = 9.0, 2.4 Hz, 1H), 7.49 – 7.36 (m, 3H), 7.30 (d, J = 9.0 Hz, 1H), 7.16 (dd, J = 12.5, 7.7 Hz, 2H), 5.25 (br.s, 1H), 3.48 – 3.38 (m, 1H), 3.08 (d, J = 17.8 Hz, 1H), 2.78 (d, J = 17.8 Hz, 1H), 2.60 (ddd, J = 19.0, 9.6, 3.5 Hz, 1H), 2.46 (dt, J = 14.1, 9.9 Hz, 1H), 2.31 – 2.14 (m, 1H), 1.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.0, 161.2, 145.5, 143.3, 142.5, 133.9, 130.2, 129.4, 129.2, 128.5, 128.1, 126.5, 126.1, 125.4, 123.8, 114.2, 101.9, 55.8, 38.4, 36.1, 30.6, 15.7; IR (neat): υ_{max} 3363, 2980, 2829, 1766, 1657, 1616, 1531, 1348, 1132, 1061, 992, 854, 773 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{19}N_2O_5$ $[M+H]^+$: 391.1288 ; found: 391.1295.

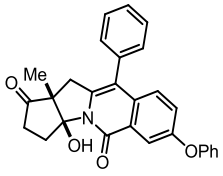
3a-Hydroxy-11a-methyl-9-phenoxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3af)

[and]

3a-Hydroxy-11a-methyl-7-phenoxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3af[1]):



3af



3af[1]

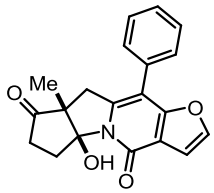
Prepared according to the general procedure as described above in 81% overall yield. Both regioisomers were seperated by flash chromatography 30% EtOAc/hexanes) to afford **3af** and **3af[1]** as white solids.

3af data: mp = 160 – 162 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (dd, J = 8.0, 0.9 Hz, 1H), 7.37 (t, J = 7.9 Hz, 1H), 7.14 (dd, J = 7.8, 0.9 Hz, 1H), 7.09 – 7.01 (m, 3H), 6.98 (dd, J = 8.3, 7.6 Hz, 2H), 6.95 – 6.89 (m, 2H), 6.81 (t, J = 7.3 Hz, 1H), 6.20 (d, J = 7.9 Hz, 2H), 5.43 (br.s, 1H), 3.34 (ddd, J = 9.4, 7.3, 4.0 Hz, 1H), 2.85 (d, J = 17.6 Hz, 1H), 2.60 – 2.49 (m, 2H), 2.44 (dt, J = 13.8, 9.6 Hz, 1H), 2.29 – 2.19 (m, 1H), 1.13 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.6, 161.8, 157.7, 151.1, 139.7, 137.8, 131.9, 129.2, 129.2, 129.1, 128.1, 127.9, 127.6,

126.9, 126.8, 125.8, 123.9, 122.0, 116.1, 112.4, 101.7, 55.6, 38.6, 36.3, 31.2, 15.9 ; IR (neat): υ_{max} 3314, 2916, 1756, 1652, 1341, 1216, 1014, 992, 864, 772 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{24}NO_4$ $[M+H]^+$: 438.1700 ; found: 438.1705.

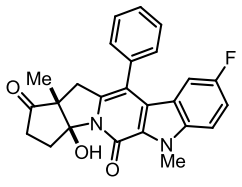
3af[1] data: mp = 165 – 167 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 2.5 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.37 – 7.32 (m, 1H), 7.32 – 7.26 (m, 2H), 7.25 – 7.21 (m, 1H), 7.20 (s, 1H), 7.17 (d, *J* = 9.8 Hz, 2H), 7.11 – 7.06 (m, 1H), 7.01 – 6.95 (m, 2H), 5.24 (br' s, 1H), 3.30 (ddd, *J* = 13.6, 9.2, 4.1 Hz, 1H), 3.03 – 2.97 (m, 1H), 2.72 (d, *J* = 17.3 Hz, 1H), 2.54 (ddd, *J* = 18.7, 9.4, 4.1 Hz, 1H), 2.42 (dt, *J* = 13.9, 9.5 Hz, 1H), 2.26 – 2.16 (m, 1H), 1.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.7, 161.7, 156.5, 156.2, 136.9, 135.0, 133.9, 130.4, 130.3, 130.0, 129.0, 128.9, 128.0, 126.8, 126.7, 124.9, 124.0, 119.4, 114.6, 114.4, 101.3, 55.9, 38.0, 36.4, 31.2, 15.7; IR (neat): υ_{max} 3314, 2916, 1756, 1652, 1534, 1435, 1341, 1216, 1014, 992, 772 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{24}NO_4$ $[M+H]^+$: 438.1700 ; found: 438.1719.

5a-Hydroxy-8a-methyl-10-phenyl-6,7,8a,9-tetrahydro-4*H*-cyclopenta[*b*]furo[3,2-*f*]indolizine-4,8(5a*H*)-dione (3ag) :



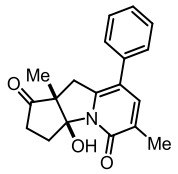
Prepared according to the general procedure as described above in 58% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp = 150 – 152 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, *J* = 2.1 Hz, 1H), 7.45 (d, *J* = 5.6 Hz, 2H), 7.43 – 7.36 (m, 3H), 7.01 (d, *J* = 2.1 Hz, 1H), 5.42 (br.s, 1H), 3.47 – 3.35 (m, 1H), 3.30 (d, *J* = 17.4 Hz, 1H), 3.02 (d, *J* = 17.4 Hz, 1H), 2.70 – 2.47 (m, 2H), 2.36 – 2.16 (m, 1H), 1.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.4, 159.8, 143.8, 141.2, 141.1, 131.4, 129.4, 128.7, 128.2, 115.6, 107.5, 107.1, 101.5, 56.3, 38.2, 36.4, 31.6, 15.8 ; IR (neat): υ_{max} 3473, 2970, 2839, 1766, 1627, 1606, 1511, 1354, 1248, 1032, 834, 773 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{18}NO_4$ $[M+H]^+$: 336.1230; found: 336.1212.

9-Fluoro-3a-hydroxy-6,12a-dimethyl-11-phenyl-3,3a,12,12a-tetrahydrocyclopenta[2,3]indolizino[6,7-b]indole-1,5(2H,6H)-dione (3ah):



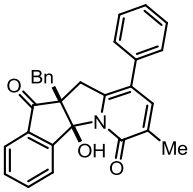
Prepared according to the general procedure as described above in 74% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp = 142 – 144°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.47 (m, 3H), 7.40 – 7.29 (m, 3H), 7.18 (td, J = 9.0, 2.5 Hz, 1H), 6.60 (dd, J = 9.7, 2.5 Hz, 1H), 5.58 (br.s, 1H), 4.33 (s, 3H), 3.41 – 3.34 (m, 1H), 3.11 (d, J = 17.0 Hz, 1H), 2.81 (d, J = 17.0 Hz, 1H), 2.70 – 2.53 (m, 2H), 2.38 – 2.27 (m, 1H), 1.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.9, 157.3 (d, J_{CF} = 236.8 Hz), 156.2, 139.4, 138.3, 135.3, 134.5, 129.9, 129.2 (d, J_{CF} = 7.0 Hz), 128.5, 127.5, 125.8, 121.0, 116.0, 115.6, 113.4, 110.9 (d, J_{CF} = 9.4 Hz), 107.9 (d, J_{CF} = 24.9 Hz), 101.9, 56.6, 37.6, 36.7, 32.0, 22.9, 16.0; IR (neat): υ_{max} 3316, 2925, 2854, 1744, 1650, 1488, 1461, 1269, 1129, 856, 759 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{22}FN_2O_3$ $[M+H]^+$: 417.1609; found: 417.1613.

3a-Hydroxy-6,9a-dimethyl-8-phenyl-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3ai):



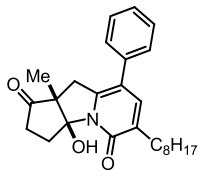
Prepared according to the general procedure as described above in 69% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp = 160 – 162 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 2H), 7.35 (d, J = 0.9 Hz, 1H), 7.32 (ddd, J = 7.4, 3.9, 1.2 Hz, 1H), 7.25 – 7.22 (m, 2H), 5.86 (br.s, 1H), 3.34 – 3.25 (m, 1H), 3.25 (d, J = 17.4 Hz, 1H), 2.98 (dd, J = 17.4, 0.7 Hz, 1H), 2.62 (ddd, J = 18.5, 9.4, 4.8 Hz, 1H), 2.51 (dt, J = 14.0, 9.2 Hz, 1H), 2.28 (dt, J = 18.3, 9.1 Hz, 1H), 2.18 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.6, 162.8, 141.5, 140.7, 136.9, 128.9, 128.3, 128.2, 127.5, 116.7, 102.0, 55.9, 38.8, 36.6, 31.6, 16.1, 16.0; IR (neat): υ_{max} 3473, 2970, 2839, 1766, 1657, 1646, 1511, 1326, 1248, 1135, 1032, 834, 773 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{20}NO_3$ $[M+H]^+$: 310.1438 ; found: 310.1447.

10a-Benzyl-4b-hydroxy-7-methyl-9-phenyl-10,10a-dihydro-4b*H*-indeno[2,1-*b*]indolizine-6,11-dione (3aj):



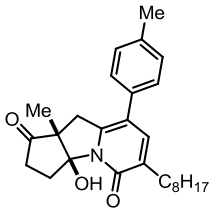
Prepared according to the general procedure as described above in 60% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 194 – 196 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, J = 8.1 Hz, 1H), 7.73 – 7.67 (m, 2H), 7.53 – 7.48 (m, 1H), 7.34 – 7.26 (m, 3H), 7.25 – 7.21 (m, 2H), 7.18 (d, J = 0.9 Hz, 1H), 7.11 – 7.05 (m, 3H), 6.96 – 6.91 (m, 2H), 3.41 (d, J = 14.0 Hz, 1H), 3.21 (d, J = 10.5 Hz, 1H), 3.15 (dd, J = 22.6, 15.7 Hz, 2H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.7, 163.1, 151.4, 141.5, 141.0, 136.6, 136.1, 136.1, 134.3, 130.9, 130.9, 128.7, 128.3, 128.0, 127.7, 127.5, 126.7, 126.7, 123.8, 116.9, 100.8, 62.0, 36.1, 35.3, 16.1; IR (neat): υ_{max} 3314, 2924, 2853, 1729, 1648, 1552, 1265, 1168, 1068, 857, 771, 741 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{24}NO_3$ $[M+H]^+$: 434.1751 ; found: 434.1776.

3a-Hydroxy-9a-methyl-6-octyl-8-phenyl-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3ak):



Prepared according to the general procedure as described above in 59% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 2H), 7.35 – 7.28 (m, 2H), 7.27 – 7.23 (m, 2H), 3.29 – 3.16 (m, 1H), 3.25 (d, J = 17.5 Hz, 1H), 2.98 (d, J = 17.5 Hz, 1H), 2.69 – 2.47 (m, 4H), 2.35 – 2.24 (m, 1H), 1.70 – 1.51 (m, 4H), 1.43 – 1.20 (m, 8H), 1.26 (s, 3H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.6, 162.5, 141.3, 139.7, 137.1, 132.7, 128.9, 128.2, 127.5, 116.6, 102.0, 55.8, 38.9, 36.6, 32.0, 31.9, 29.8, 29.7, 29.6, 29.4, 28.8, 22.8, 16.0, 14.2; IR (neat): υ_{max} 3315, 2925, 2854, 1746, 1647, 1589, 1553, 1454, 1269, 1145, 1072, 770, 701 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{33}NO_3Na$ $[M+Na]^+$: 430.2353 ; found: 430.2375.

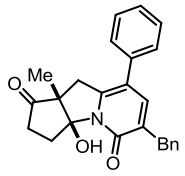
3a-Hydroxy-9a-methyl-6-octyl-8-(*p*-tolyl)-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3al):



Prepared according to the general procedure as described above in 64% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow oil ; ^{1}H NMR (300 MHz,

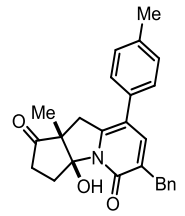
$CDCl_3$) δ 7.29 (s, 1H), 7.21 (d, J = 7.9 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 5.84 (br.s, J = 12.8 Hz, 1H), 3.28 – 3.21 (m, 1H), 3.24 (d, J = 17.4 Hz, 1H), 2.96 (d, J = 17.4 Hz, 1H), 2.71 – 2.45 (m, 4H), 2.38 (s, 3H), 2.42 – 2.22 (m, 1H), 1.78 – 1.52 (m, 4H), 1.46 – 1.16 (m, 8H), 1.25 (s, 3H) , 0.87 (t, J = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.6, 162.5, 141.1, 139.8, 137.3, 134.1, 132.6, 129.5, 128.1, 116.5, 102.0, 55.8, 38.9, 36.6, 32.0, 31.9, 29.8, 29.7, 29.6, 29.4, 28.8, 22.8, 21.3, 16.0, 14.2; IR (neat): υ_{max} 3315, 2935, 2814, 1732, 1654, 1559, 1553, 1464, 1145, 1032, 772, 701 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{36}NO_3$ $[M+H]^+$: 422.2690; found: 422.2699.

6-Benzyl-3a-hydroxy-9a-methyl-8-phenyl-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3am):



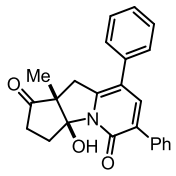
Prepared according to the general procedure as described above in 64% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp = 203 – 205°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 2H), 7.33 – 7.25 (m, 5H), 7.24 – 7.14 (m, 4H), 5.65 (s, 1H), 3.91 (q, J = 15.6 Hz, 2H), 3.29 – 3.23 (m, 1H), 3.25 (d, J = 17.4 Hz, 1H), 2.97 (d, J = 17.5 Hz, 1H), 2.64 (ddd, J = 18.5, 9.4, 5.0 Hz, 1H), 2.52 (dt, J = 14.1, 9.1 Hz, 1H), 2.30 (dt, J = 18.2, 9.0 Hz, 1H), 1.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.5, 162.2, 142.0, 140.6, 139.4, 136.9, 131.7, 129.3, 128.9, 128.7, 128.2, 127.5, 126.5, 116.6, 102.1, 55.8, 38.9, 36.6, 35.7, 31.8, 16.0; IR (neat): υ_{max} 3314, 2926, 1745, 1647, 1588, 1441, 1308, 1217, 1165, 1052, 872, 772 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{24}NO_3$ $[M+H]^+$: 386.1751; found: 386.1764.

6-Benzyl-3a-hydroxy-9a-methyl-8-(p-tolyl)-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3an):



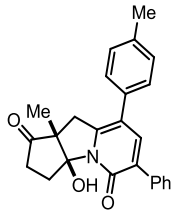
Prepared according to the general procedure as described above in 65% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a yellow solid; mp = 174 – 176 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.25 (m, 5H), 7.24 – 7.19 (m, 1H), 7.19 – 7.15 (m, 2H), 7.06 (d, J = 8.1 Hz, 2H), 3.90 (q, J = 15.6 Hz, 2H), 3.28 - 3.20 (m, 1H), 3.24 (d, J = 17.5 Hz, 1H), 2.95 (d, J = 17.5 Hz, 1H), 2.63 (ddd, J = 18.5, 9.4, 5.1 Hz, 1H), 2.56 – 2.49 (m, 1H), 2.38 – 2.26 (m, 1H), 2.35 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.5, 162.2, 141.8, 140.7, 139.4, 137.4, 133.9, 131.6, 129.5, 129.3, 128.7, 128.1, 126.5, 116.6, 102.1, 55.8, 38.9, 36.6, 35.7, 31.8, 21.2, 16.0; IR (neat): υ_{max} 3324, 2936, 1786, 1652, 1589, 1421, 1325, 1216, 1136, 1065, 890, 775 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{26}NO_3$ $[M+H]^+$: 400.1907 ; found: 400.1931.

3a-Hydroxy-9a-methyl-6,8-diphenyl-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3ao):



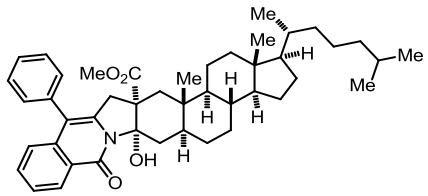
Prepared according to the general procedure as described above in 65% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a yellow solid; mp = 177 – 179 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 – 7.70 (m, 2H), 7.66 (s, 1H), 7.50 – 7.27 (m, 8H), 5.89 (br.s, 1H), 3.40 – 3.29 (m, 1H), 3.35 (d, J = 17.7 Hz, 1H), 3.06 (d, J = 17.7 Hz, 1H), 2.73 – 2.48 (m, 2H), 2.42 – 2.27 (m, 1H), 1.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.5, 161.4, 143.6, 141.2, 136.7, 135.8, 130.5, 129.0, 128.8, 128.4, 128.3, 128.1, 127.7, 117.3, 102.6, 55.7, 39.1, 36.6, 31.8, 16.1; IR (neat): υ_{max} 3314, 2936, 1756, 1622, 1632, 1451, 1435, 1316, 1215, 1125, 890, 775 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{21}NO_3Na$ $[M+Na]^+$: 394.1414; found: 394.1416.

3a-Hydroxy-9a-methyl-6-phenyl-8-(*p*-tolyl)-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3ap):



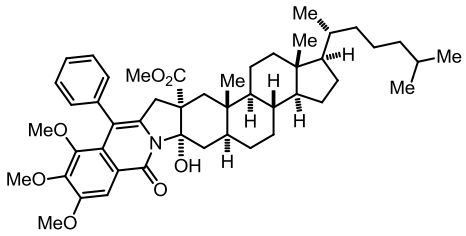
Prepared according to the general procedure as described above in 68% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a white solid; mp = 223 – 225 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 – 7.69 (m, 2H), 7.64 (s, 1H), 7.48 – 7.32 (m, 3H), 7.29 – 7.17 (m, 4H), 5.92 (s, 1H), 3.40 – 3.26 (m, 1H), 3.34 (d, J = 17.4 Hz, 1H), 3.04 (d, J = 17.7 Hz, 1H), 2.73 – 2.49 (m, 2H), 2.46 – 2.26 (m, 1H), 2.40 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.4, 161.4, 143.3, 141.3, 137.6, 135.9, 133.7, 130.4, 129.7, 128.8, 128.4, 128.1, 128.0, 117.2, 102.6, 55.7, 39.1, 36.6, 31.9, 21.3, 16.1; IR (neat): υ_{max} 3345, 2961, 1756, 1642, 1593, 1420, 1211, 1146, 1048, 894, 771 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{23}NO_3Na$ [M+Na]$^+$: 408.1570 ; found 408.1559.

Compound 5a data:



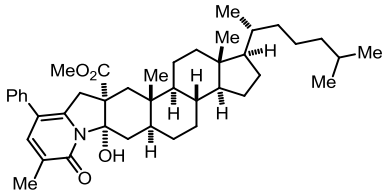
Prepared according to the general procedure as described above in 61% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford a yellow oil; $[\alpha]^{25}_D$ = -26.0 (c = 0.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (dd, J = 8.0, 1.0 Hz, 1H), 7.55 – 748 (m, 2H), 7.48 – 7.40 (m, 3H), 7.37 (d, J = 7.3 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.18 (d, J = 7.7 Hz, 1H), 4.52 (br.s, 1H), 3.73 (s, 3H), 3.72(d, J = 14.2 Hz, 1H), 3.22 (d, J = 15.7 Hz, 1H), 2.54 (d, J = 15.7 Hz, 1H), 2.31 (d, J = 14.2 Hz, 1H), 2.12 (dd, J = 13.6, 12.7 Hz, 1H), 1.91 (ddd, J = 12.5, 2.9, 2.9 Hz, 1H), 1.77 (ddd, J = 15.2, 12.1, 7.7 Hz, 1H), 1.68 – 1.57 (m, 2H), 1.57 – 1.44 (m, 3H), 1.43 – 1.25 (m, 8H), 1.24 – 1.16 (m, 2H), 1.14 – 1.03 (m, 5H), 1.02 – 0.95 (m, 2H), 0.90 –0.87 (m, 1H), 0.86 (d, J = 6.1 Hz, 3H), 0.85 (d, J = 1.8 Hz, 3H), 0.84 (d, J = 1.8 Hz, 3H), 0.81 (s, 3H), 0.61 (s, 3H), 0.52 (td, J = 12.3, 3.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.1, 162.3, 139.2, 137.8, 136.0, 132.4, 131.0, 130.6, 129.1, 128.9, 128.3, 127.8, 126.9, 126.1, 124.3, 115.6, 96.7, 56.4, 56.3, 54.1, 52.5, 51.7, 47.3, 43.6, 42.7, 40.0, 39.6, 38.7, 36.2, 36.2, 35.9, 35.2, 35.2, 31.6, 28.3, 28.1, 27.5, 24.2, 24.0, 23.0, 22.7, 21.5, 18.8, 12.4, 12.2. IR (neat): υ_{max} 3373, 3042, 2960, 2839, 1766, 1652, 1646, 1531, 1348, 1232, 1062, 998, 856, 834, 773 cm^{-1}; HRMS (ESI) calcd for $C_{45}H_{59}NO_4Na$ [M+Na]$^+$: 700.4336; found: 700.4345.

Compound 5b data:



Prepared according to the general procedure as described above in 67% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford yellow oil; $[\alpha]^{25}_{D}$ = -32.0 (*c* = 0.45, $CHCl_3$); 1H NMR (500 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.43 (td, *J* = 7.3, 1.6 Hz, 1H), 7.39 – 7.31 (m, 3H), 7.21 (dt, *J* = 5.3, 1.4 Hz, 1H), 3.98 (s, 3H), 3.86 (s, 3H), 3.70 (s, 3H), 3.66 (d, *J* = 2.3 Hz, 1H), 3.16 (s, 3H), 3.02 (d, *J* = 15.8 Hz, 1H), 2.34 (d, *J* = 15.8Hz, 1H), 2.28 (d, *J* = 14.2 Hz, 1H), 2.12 – 2.06 (m, 1H), 1.95 – 1.89 (m, 1H), 1.82 – 1.74 (m, 1H), 1.70 – 1.59 (m, 7H), 1.53 – 1.46 (m, 2H), 1.38 – 1.28 (m, 5H), 1.24 (d, *J* = 2.7 Hz, 1H), 1.22 – 1.15 (m, 2H), 1.10 (dd, *J* = 16.7, 9.5 Hz, 2H), 1.04 (d, *J* = 14.4 Hz, 1H), 0.98 (dd, *J* = 19.4, 10.0 Hz, 1H), 0.87 (d, *J* = 4.4 Hz, 2H), 0.85 (d, *J* = 2.3 Hz, 6H), 0.84 (d, *J* = 2.2 Hz, 3H), 0.78 (s, 3H), 0.61 (s, 3H), 0.53 (ddd, *J* = 14.4, 10.4, 3.9 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.2, 161.4, 152.5, 149.0, 147.4, 139.6, 138.2, 129.8, 129.8, 128.0, 128.0, 126.7, 123.6, 113.5, 105.2, 96.9, 61.0, 60.8, 56.4, 56.3, 54.0, 52.4, 51.5, 47.1, 43.5, 42.7, 40.0, 39.6, 38.9, 36.2 (2C), 35.9, 35.3, 35.1, 32.1, 31.6, 28.3, 28.1, 27.5, 24.2, 24.0, 23.0, 22.7, 21.4, 18.8, 12.3, 12.2; IR (neat): υ_{max} 3353, 3046, 2970, 2815, 1752, 1652, 1631, 1558, 1321, 1262, 1156, 1041, 985, 878, 824, 773 cm^{-1}; HRMS (ESI) calcd for $C_{48}H_{65}NO_7Na$ $[M+Na]^+$: 790.4653; found: 790.4696.

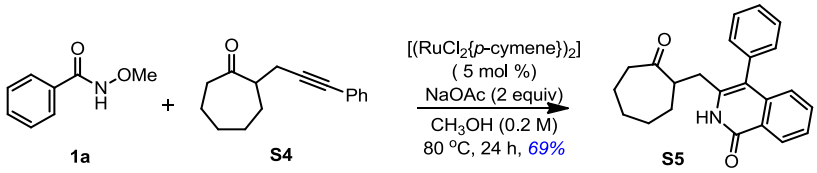
Compound 5c data:



Prepared according to the general procedure as described above in 58% yield. It was purified by flash chromatography (20% EtOAc/hexanes) to afford colorless oil; $[\alpha]^{25}_{D}$ = -29.0 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.38 (m, 2H), 7.34 – 7.27 (m, 4H), 3.76 (s, 3H), 3.70 (dd, *J* = 14.2, 2.4 Hz, 1H), 3.43 (d, *J* = 15.6 Hz, 1H), 2.73 (d, *J* = 15.7 Hz, 1H), 2.27 (d, *J* = 14.2 Hz, 1H), 2.16 (s, 3H), 2.12 – 2.05 (m, 1H), 1.94 – 1.85 (m, 2H), 1.83 – 1.69

(m, 2H), 1.66 – 1.58 (m, 2H), 1.55 – 1.45 (m, 2H), 1.38 – 1.27 (m, 5H), 1.25 – 1.18 (m, 3H), 1.16 – 1.05 (m, 3H), 1.03 – 0.96 (m, 3H), 0.94 – 0.91 (m, 1H), 0.87 (d, *J* = 7.5, 1.4 Hz, 2H), 0.85 (d, *J* = 2.3 Hz, 6H), 0.84 (d, *J* = 2.4 Hz, 3H), 0.79 (s, 3H), 0.60 (s, 3H), 0.50 (td, *J* = 12.3, 3.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 162.9, 142.2, 139.1, 137.7, 129.7, 128.8, 128.4, 127.2, 116.9, 97.3, 56.5, 56.3, 54.2, 52.5, 52.0, 47.6, 43.5, 42.7, 39.9, 39.6, 39.1, 36.3, 36.1, 35.9, 35.2, 34.8, 31.6, 28.3, 28.1, 27.4, 24.3, 24.0, 23.0, 22.7, 21.5, 18.8, 17.0, 12.5, 12.2; IR (neat): υ_{max} 3385, 3054, 2998, 2853, 1762, 1648, 1626, 1558, 1368, 1236, 1162, 1032, 992, 856, 834, 772 cm^{-1}; HRMS (ESI) calcd for $C_{42}H_{59}NO_4Na$ $[M+Na]^+$: 642.1517; found: 642.4560.

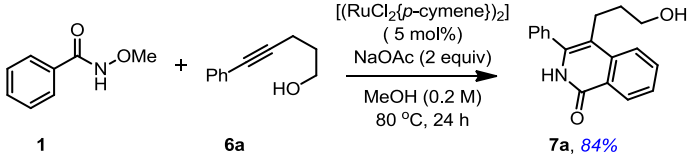
3-((2-Oxocycloheptyl)methyl)-4-phenylisoquinolin-1(2H)-one (S5):



1a S4 S5

Prepared according to the general procedure as described above in 69% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 122 – 124 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 7.79 – 7.68 (m, 2H), 7.56 – 7.37 (m, 6H), 3.23 (dd, *J* = 14.3, 4.3 Hz, 1H), 2.74 (dd, *J* = 23.4, 9.0 Hz, 1H), 2.70 – 2.59 (m, 1H), 2.36 – 2.19 (m, 2H), 1.72 – 1.54 (m, 3H), 1.53 – 1.33 (m, 2H), 1.34 – 1.19 (m, 1H), 1.17 – 0.94 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.4, 162.5, 138.6, 137.8, 135.4, 133.0, 129.7, 129.4, 129.1, 128.3, 126.7, 126.0, 123.8, 111.6, 52.4, 42.4, 29.9, 29.3, 28.3, 27.6, 25.0; IR (neat) : υ_{max} 3473, 3315, 2964, 2869, 1765, 1656, 1554, 1342, 1218, 1016, 892, 834, 773 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{23}NO_4Na$ $[M+Na]^+$: 368.1621; found: 368.1640.

4-(3-Hydroxypropyl)-3-phenylisoquinolin-1(2*H*)-one (7a):[16]

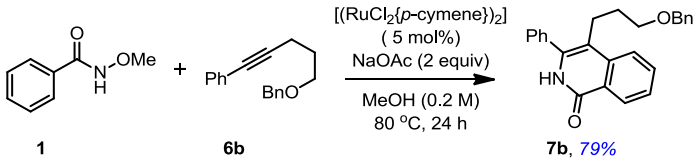


1 6a 7a, 84%

Prepared according to the general procedure as described above in 84% yield. It was purified by flash chromatography (50% EtOAc/hexanes) to afford a white solid; mp = 136 – 138 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.49 (d, *J* = 7.9 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H),

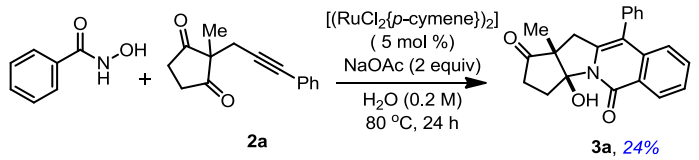
7.76 (t, *J* = 7.7 Hz, 1H), 7.58 – 7.42 (m, 6H), 3.59 (t, *J* = 6.2 Hz, 2H), 2.77 (t, *J* = 8.0 Hz, 2H), 1.89 – 1.78 (m, 2H), 1.70 (brs, 1H).; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 137.6, 136.8, 135.0, 132.8, 129.2, 128.8, 128.7, 127.9, 126.4, 125.4, 123.5, 113.8, 62.0, 33.0, 23.3; IR (neat): υ_{max} 3402, 2879, 2736, 1659, 1539, 1485, 1208, 1036, 782 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{18}NO_2$ $[M+H]^+$: 280.1332; found: 280.1339.

4-(3-(Benzyloxy)propyl)-3-phenylisoquinolin-1(2*H*)-one (7b):



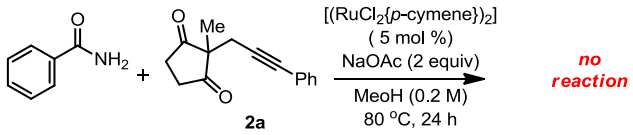
Prepared according to the general procedure as described above in 79% yield. It was purified by flash chromatography (30% EtOAc/hexanes) to afford a white solid; mp = 202 – 204 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.25 (s, 1H), 8.35 (d, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.47 – 7.32 (m, 6H), 7.30 – 7.15 (m, 5H), 4.34 (s, 2H), 3.35 (t, *J* = 6.1 Hz, 2H), 2.76 – 2.64 (m, 2H), 1.85-1.72(m, 2H).; ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3, 137.5, 136.9, 136.2, 134.3, 131.8, 128.2, 128.0, 127.8, 127.3, 126.9, 126.4, 125.4, 122.8, 112.8, 71.8, 68.8, 29.6, 23.0.; IR (neat): υ_{max} 3411, 2881, 2724, 1650, 1636, 1533, 1475, 1218, 1035, 731 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{24}NO_2$ $[M+H]^+$: 370.1802; found: 370.1820.

Annulation reaction by NH-free hydroxamic acid in water:[17]



A screw-cap vial equipped with stirred bar was charged with 2-acetylenic ketone **2a** (100 mg, 0.44 mmol), *N*-hydroxybenzamide (91 mg, 0.66 mmol, 1.5 equiv), $[RuCl_2(p\text{-cymene})]_2$ (14 mg, 5.0 mol %) and NaOAc (73 mg, 0.88 mmol, 2 equiv) and water (2.2 mL) under nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 24 hours. Afterwards, it was cooled to room temperature, extracted with EtOAc (2 x 10 mL), dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (20% of EtOAc in hexane) to give the desired product **3a** in 24% yield (37 mg) as white solid.

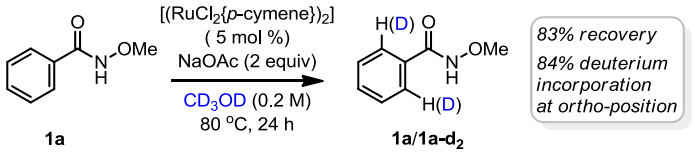
Annulation reaction with simple benzamide:



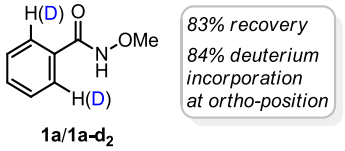
A screw-cap vial equipped with stirred bar was charged with 2-acetylenic ketone **2** (0.4 mmol), benzamide (0.6 mmol, 1.5 equiv), $[RuCl_2(p\text{-cymene})]_2$ (18.4 mg, 0.03 mmol, 5.0 mol %) and NaOAc (98.4 mg, 1.2 mmol, 2 equiv) and dry MeOH (2 mL) under nitrogen atmosphere. The reaction mixture was stirred at 80 ^oC for 24 hours. Reaction was not proceeded and starting material **2a** was recovered.

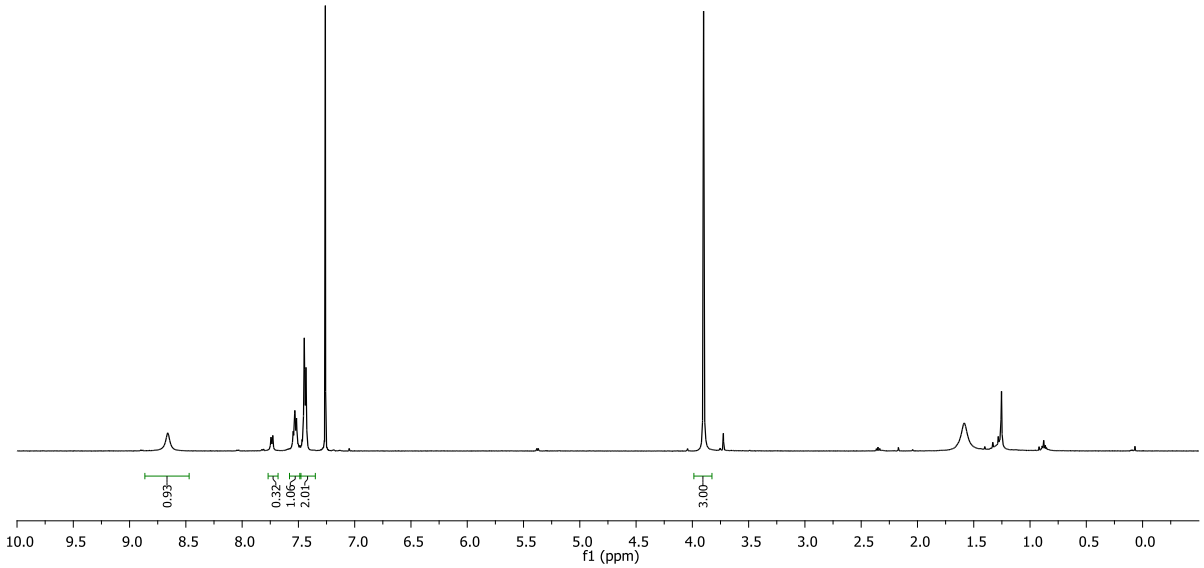
III. Deuterium-Labeling Experiments

IIIa. Deuterium Incorporation Experiments A:

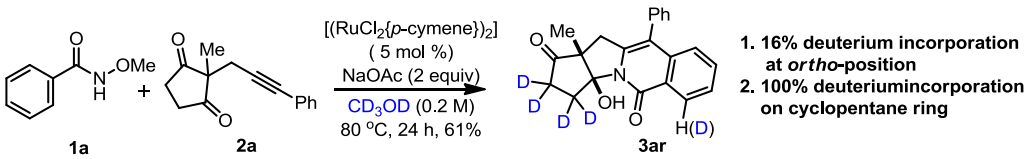


A screw-cap vial equipped with stirred bar was charged with *N*-methoxybenzamide **1a** (0.4 mmol), $[RuCl_2(p\text{-cymene})]_2$ (18.4 mg, 0.03 mmol, 5.0 mol %) and NaOAc (98.4 mg, 1.2 mmol, 2 equiv) and dry CD_3OD (2 mL) under nitrogen atmosphere. The reaction mixture was stirred at 80 ^oC for 24 hours. Afterwards, it was cooled to room temperature and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silical gel (hexanes/EtOAc: 2/1) to give the desired product **1a/1a-d$_2$** as white solid in 83% yield with 84% deuterium incorporation in the *ortho*-position, as estimated ^1H NMR spectroscopy.

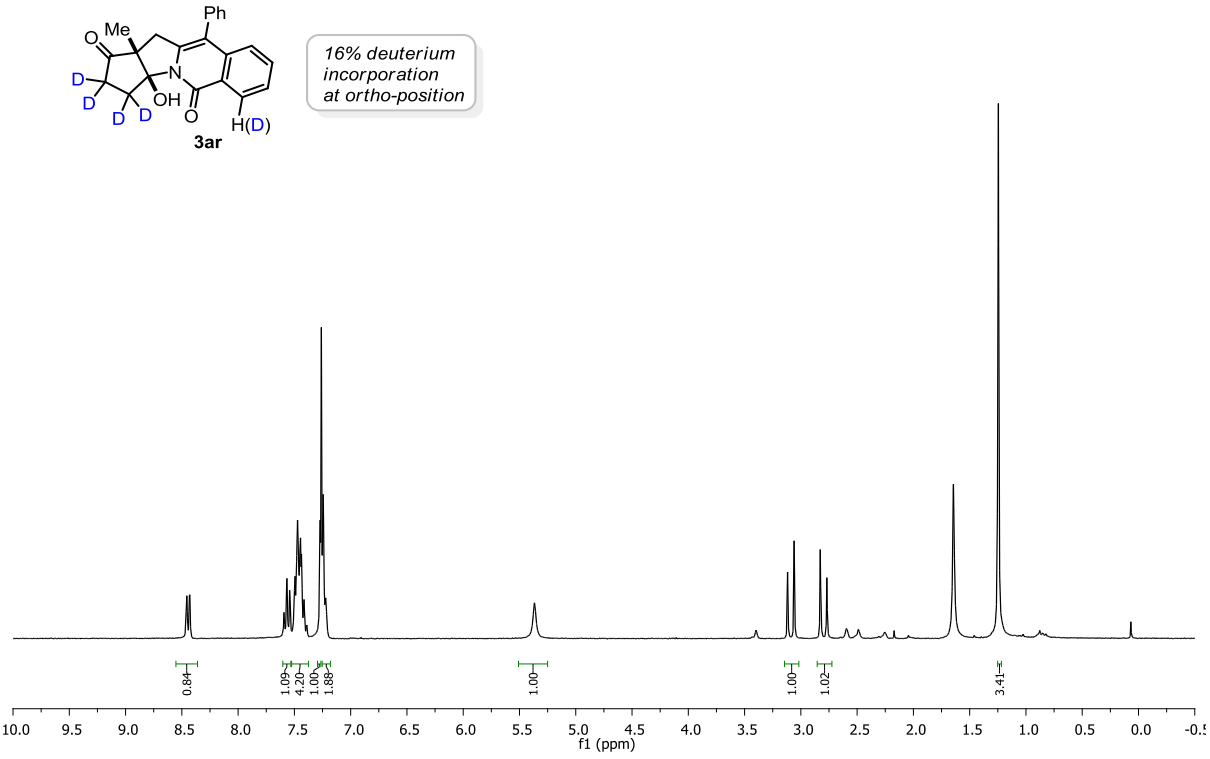




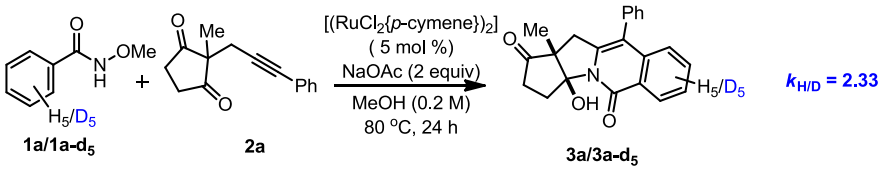
IIIb. Deuterium Incorporation Experiments B:



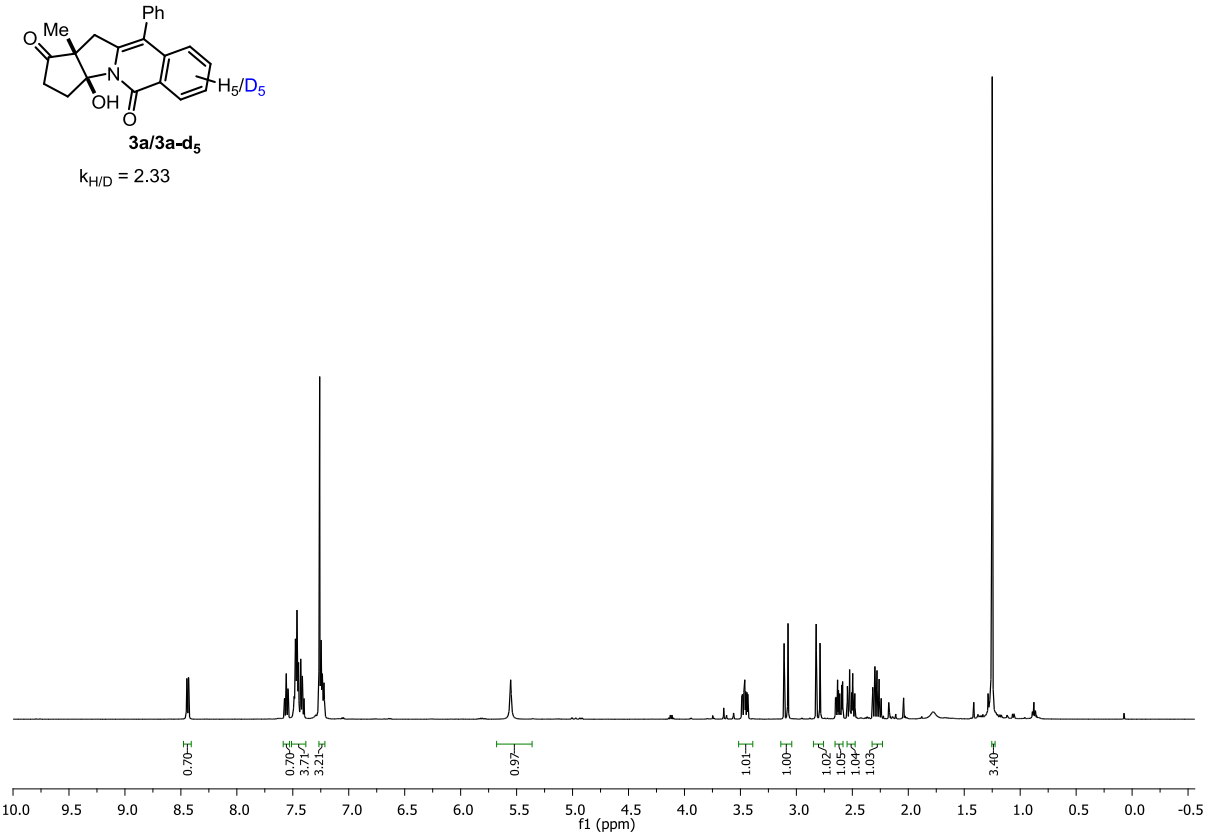
A screw-cap vial equipped with stirred bar was charged with 2-acetylenic ketone **2a** (0.4 mmol), N-methoxybenzamide **1a** (0.6 mmol, 1.5 equiv), $[RuCl_2(p\text{-cymene})]_2$ (18.4 mg, 0.03 mmol, 5.0 mol %) and NaOAc (98.4 mg, 1.2 mmol, 2 equiv) and dry CD_3OD (2 mL) under nitrogen atmosphere. The reaction mixture was stirred at 80 ^oC for 24 hours. Afterwards, it was cooled to room temperature and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc: 3/1) to give the product **3ar** in 61% yield as a colorless oil with 16% deuterium incorporation in the *ortho*-position of the benzene ring and almost full deuteration on the cyclopentane ring, as estimated ^1H NMR spectroscopy.



IIIc. Intermolecular Competition Experiment between Benzamides 1a and 1a-d_5:



A screw-cap vial equipped with stirred bar was charged with a mixture of 2-acetylenic ketone **2** (0.4 mmol, 1.0 equiv), *N*-methoxybenzamide **1a** (mg, 0.4 mmol, 1.0 equiv), *N*-methoxy-2,3,4,5,6-pentadeuteriobenzamide **1a-*d*$_5$** (78.1 mg, 0.50 mmol, 1.0 equiv), [$RuCl_2$(*p*-cymene)]$_2$ (18.4 mg, 0.03 mmol, 5.0 mol %) and NaOAc (98.4 mg, 1.2 mmol, 2 equiv) and dry MeOH (2 mL) under nitrogen atmosphere. The reaction mixture was stirred at 80 ^oC for 24 hours. Afterwards, it was cooled to room temperature and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silical gel (hexanes/EtOAc: 2/1) to give the desired product as mixture of **3a** and **3a-*d*$_5$** in 69% yield. The kinetic isotopic effect of this reaction was thus determined to be $k_H/k_D \approx 2.3$ utilizing ^{1}H NMR spectroscopy.



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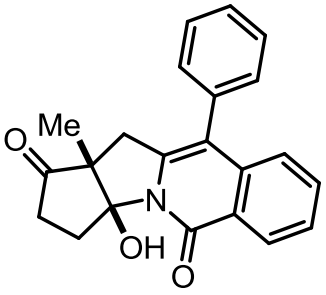
17. F. Yang and L. Ackermann, *J. Org. Chem.*, 2014, **79**, 12070.

V. X-ray crystallographic data



Compound 3a

Crystallographic data

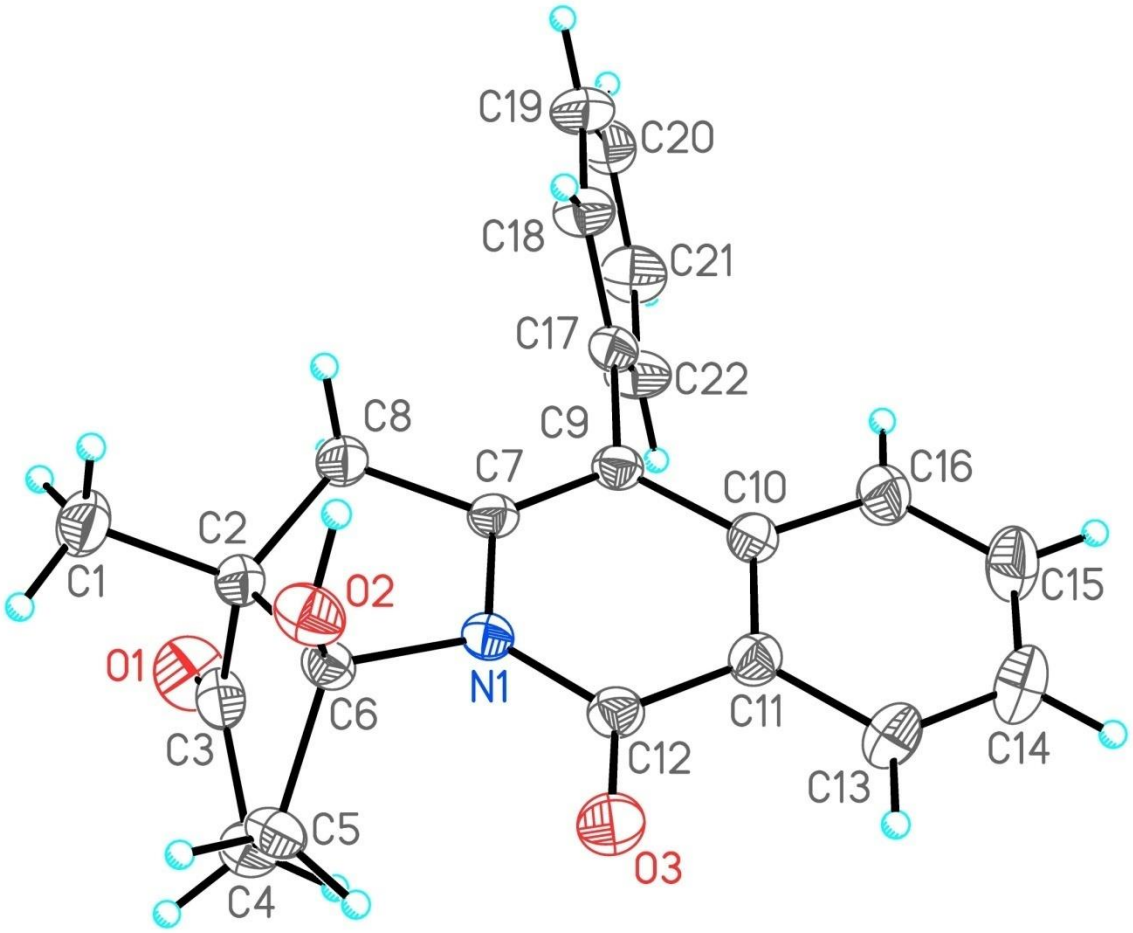


Figure caption: ORTEP diagram of compound **3a** with the atom-numbering. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius.

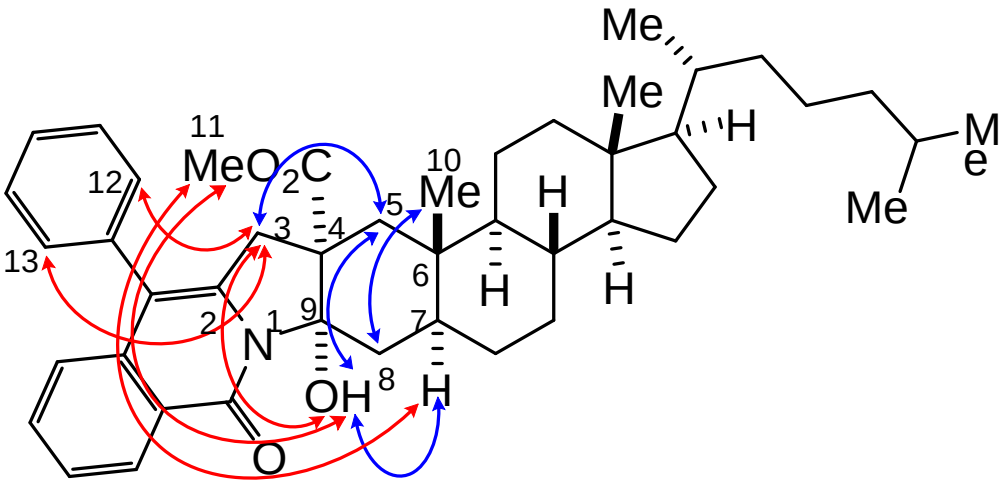
Crystal data for compound **3a**: $C_{22}H_{19}NO_2$, M = 345.38, colorless block, 0.42 x 0.32 x 0.25 mm^3, orthorhombic, space group *Pbca*, a =18.7479(11), b = 9.6392(6), c = 19.3565(11) Å, α = 90, β = 90, γ = 90°, V = 3498.0(4) $Å^3$, Z = 8, Dc = 1.312 g/cm^3, F_{000} = 1456, CCD area detector, MoKα radiation, λ = 0.71073 Å, T = 293(2)K, $2\theta_{max}$ = 56.56, 38604 reflections collected, 4295 unique (R_{int} = 0.024), Final *GooF* = 1.04, $R1$ = 0.0440, $wR2$ = 0.1297, R indices based on 3486 reflections with $I > 2\sigma(I)$ (refinement on F^2), 240 parameters, μ = 0.087 mm^{-1}. CCDC 1449113 contains supplementary crystallographic data for the structure. This data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.

Data collection and Structure solution: X-ray data for compound **3a** were collected at room temperature using the Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) with ω-scan method.[1] Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 6727 reflections. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL-2014/7.[2] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms.

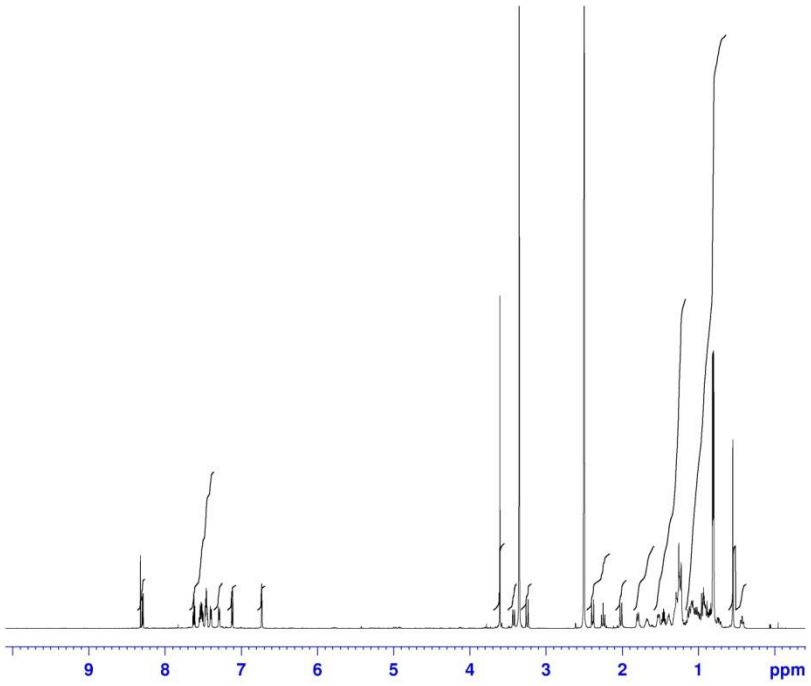
1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. SHELXS97 and SHELXL-2014/7, Programs for crystal structure solution and refinement; University of Gottingen: Germany, 2014.

VI. NOE interactions of compound 5a:

The absolute stereochemistry of the newly generated stereo centers C4 and C9 were elucidated by using 1D and 2D NMR experiments. Since, the C9 center is quaternary and contains hydroxyl group, we intended to perform NMR experiments in DMSO-*d*6 solvent to reduce the exchange rate of hydroxyl proton so that it should appear as sharp line. The proton chemical shift assignments were carried out using DQFCOSY and NOESY / ROESY experiments. The appearance of long range nOe cross correlations between OH9 / H3, OH9 / Me11, OH9 / H7, H3/H12, H3/H13 and a medium range correlations between H3/H5, OH9/ H5, H8 / Me10, OH9 / H7 strongly support for the cis orientation between OH and CO2Me as pictorially represented in compound **5a**.



Compound **5a**

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Current Data Parameters
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EXPNO                    1
PROCNO                   1

F2 - Acquisition Paramete
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Time                 21.36
INSTRUM              spect
PROBHD   5 mm CPTCI 1H-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                      128
DS                        0
SWH                7936.508 H
FIDRES             0.121101 H
AQ                 4.1288180 s
RG                      12.7
DW                     63.000 u
DE                      6.50 u
TE                     298.2 K
D1                1.00000000 s
TD0                       1

======== CHANNEL f1 =====
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P1                      6.93 u
PL1                     2.60 d
PL1W              6.62584448 W
SFO1              600.3332394 M

F2 - Processing paramete
SI                        32768
SF                600.3300057 M
WDW                          no
SSB       0
LB        0 Hz
GB        0
PC                        4.00
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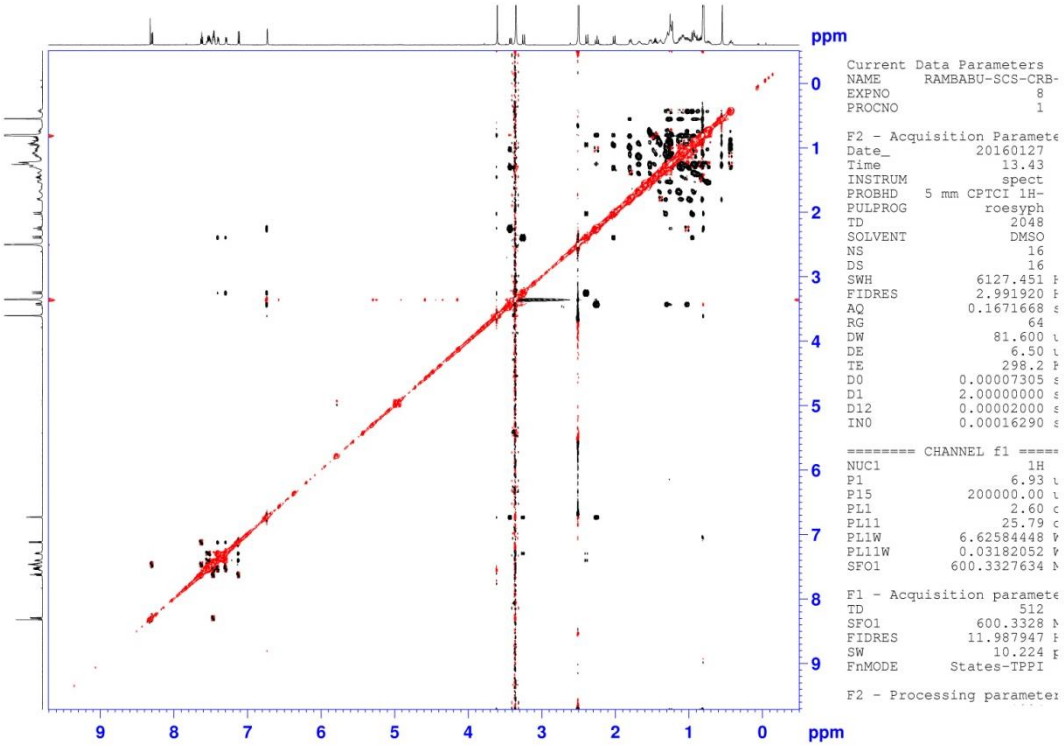
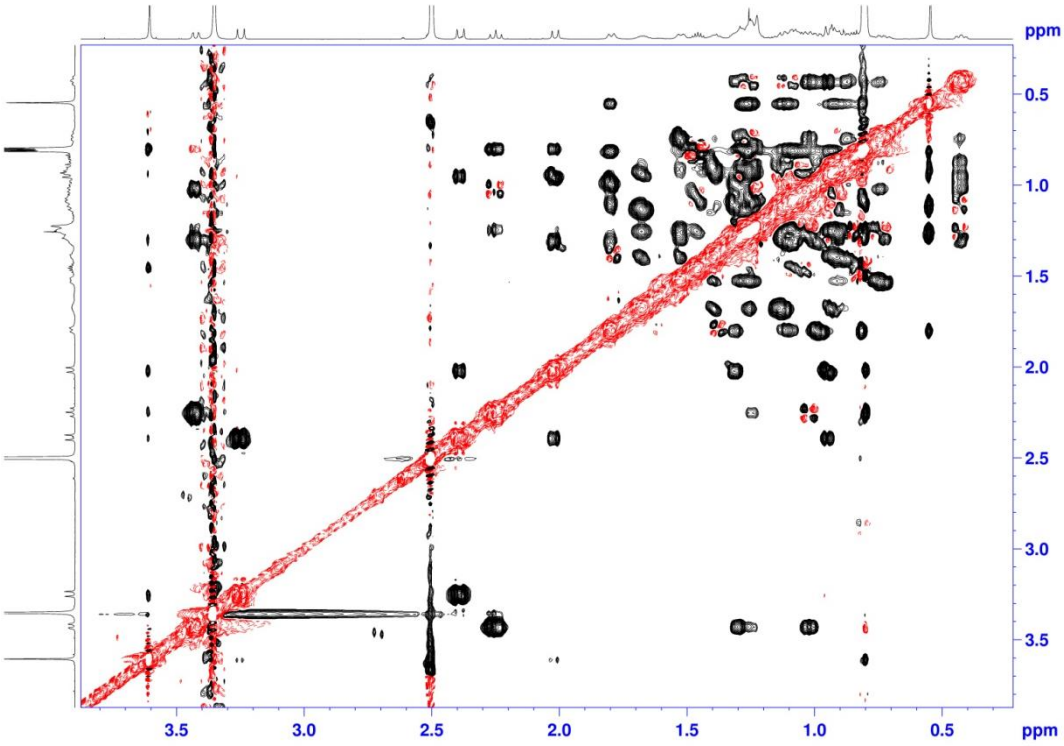
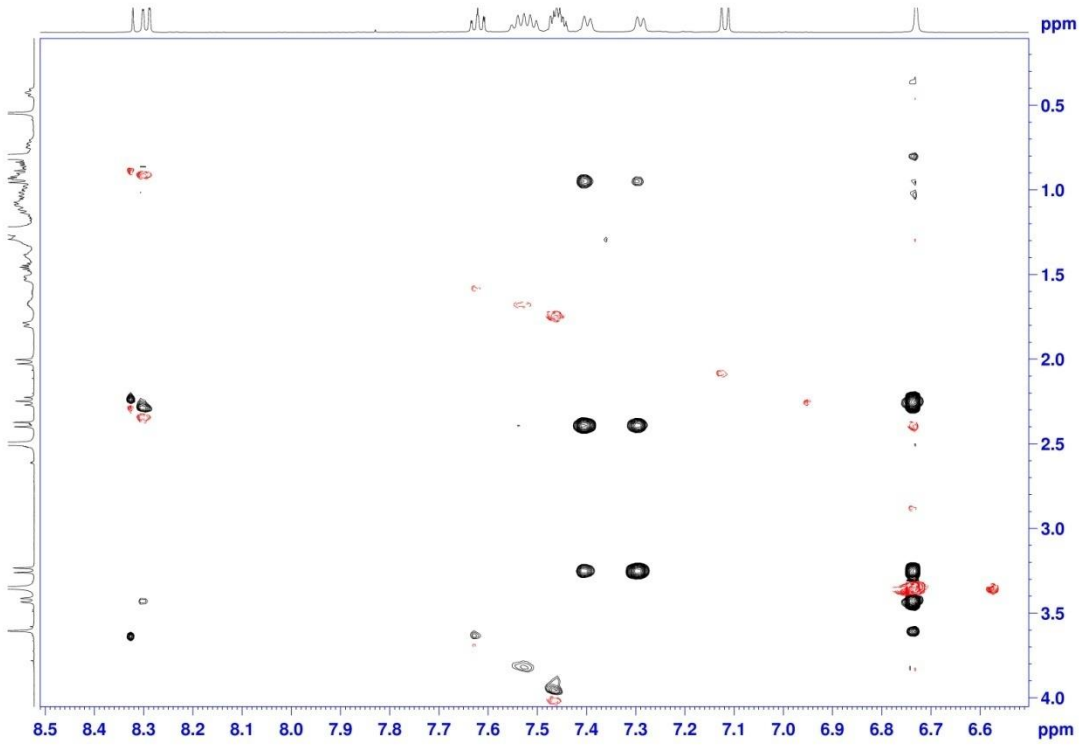
^{1}H NMR spectrum of 5a recorded in DMSO-*d*6 on 600 MHz at 25 °C.



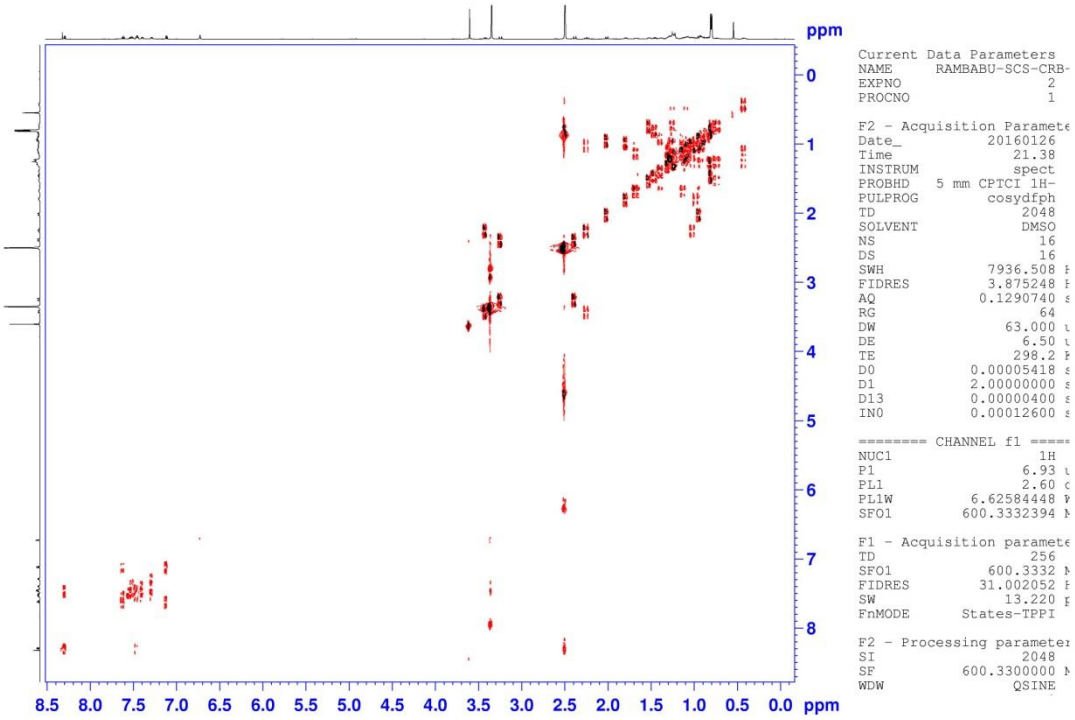
^{1}H-^{1}H 2D-ROESY (Rotating frame Overhauser effect spectroscopy) spectrum of **5a** recorded in DMSO-d6 on 600 MHz at 25 °C.



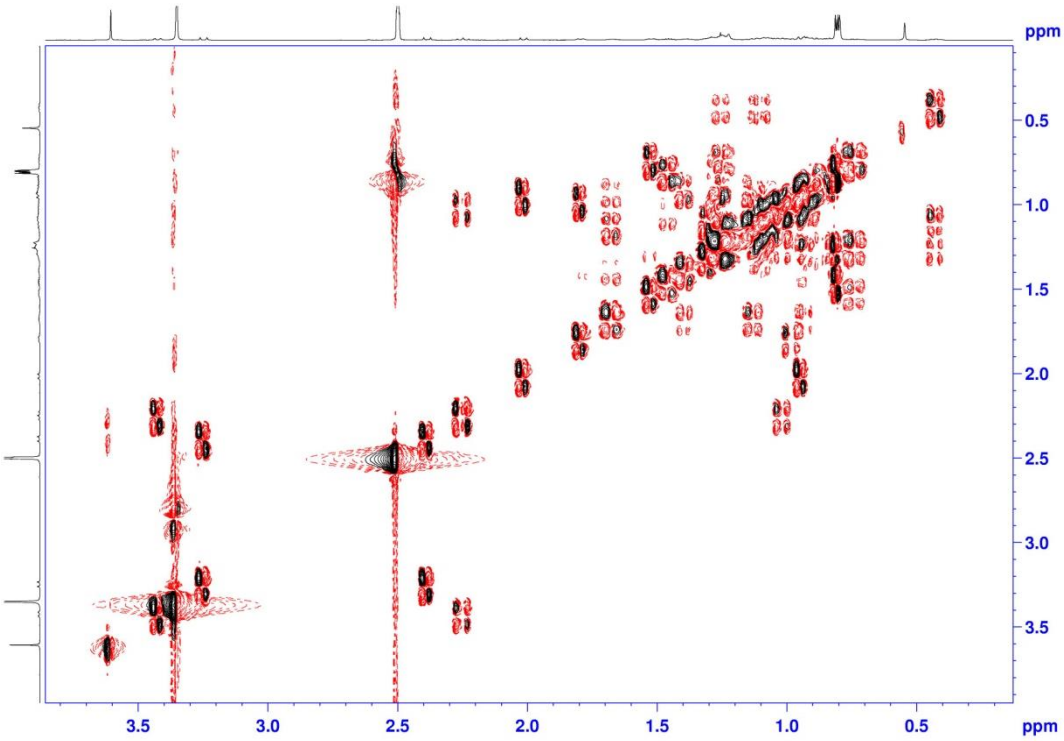
Expansion of ^{1}H-^{1}H 2D-ROESY (Rotating frame Overhauser effect spectroscopy) spectrum of **5a.**



Expansion of ^{1}H-^{1}H 2D-ROESY (Rotating frame Overhauser effect spectroscopy) spectrum of **5a.**



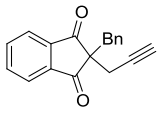
^{1}H-^{1}H 2D-DQFCOSY (Double Quantum filtered correlation spectroscopy) spectrum of **5a** recorded in DMSO-d6 on 600 MHz at 25 °C.



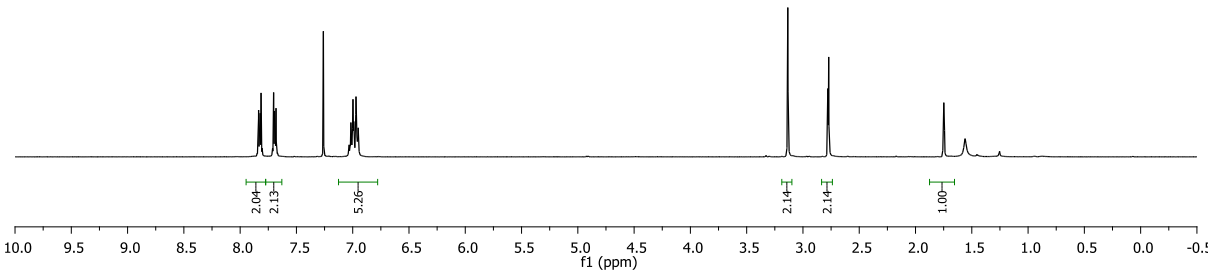
Expansion of ^{1}H-^{1}H 2D-DQFCOSY (Double Quantum filtered correlation spectroscopy) spectrum of **5a.**

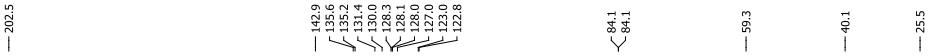
VII. ^{1}H NMR, ^{13}C NMR spectra:

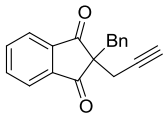
2-Benzyl-2-(prop-2-yn-1-yl)-1H-indene-1,3(2*H*)-dione (S3) :



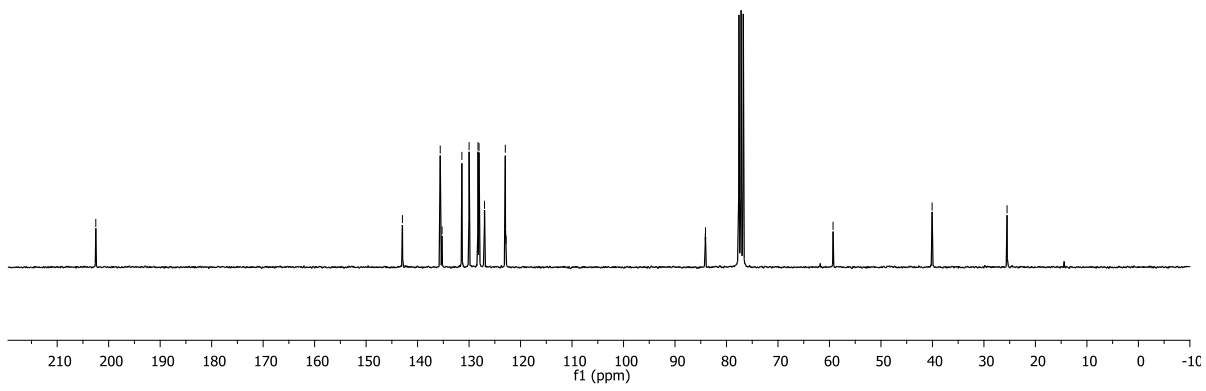
(^{1}H NMR, $CDCl_3$, 400MHz)



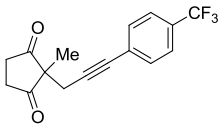




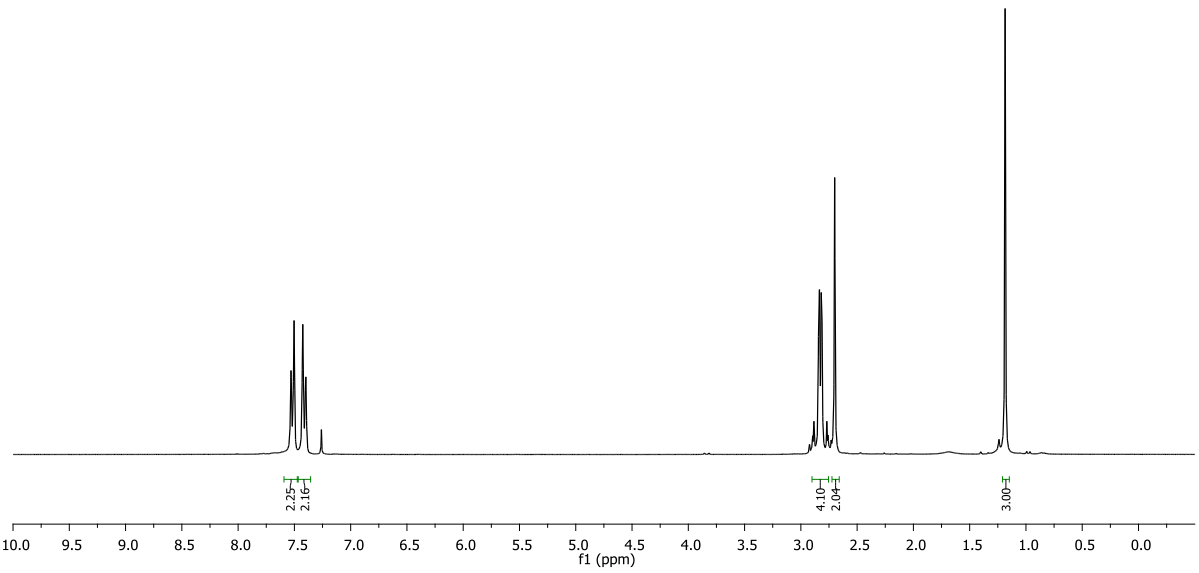
(^{13}C NMR, $CDCl_3$, 75 MHz)

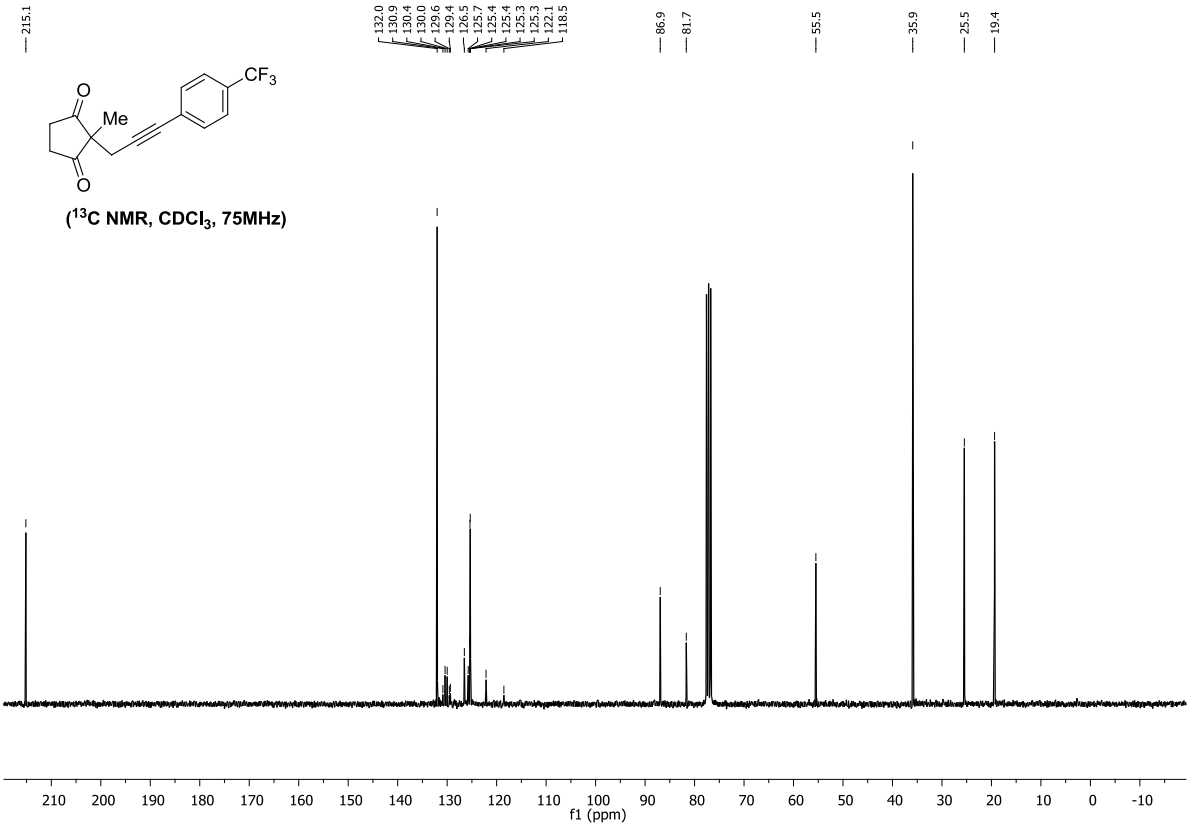


2-Methyl-2-(3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)cyclopentane-1,3-dione (2f):



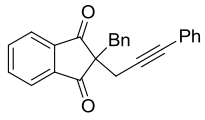
(^{1}H NMR, $CDCl_3$, 300MHz)



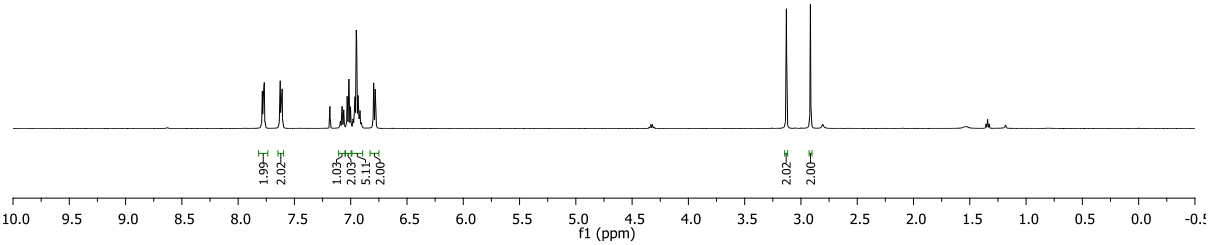


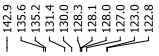
(^{13}C NMR, $CDCl_3$, 75MHz)

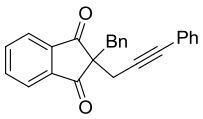
2-Benzyl-2-(3-phenylprop-2-yn-1-yl)-1H-indene-1,3(2*H*)-dione (2k):



(^{1}H NMR, $CDCl_3$, 500 MHz)

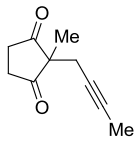




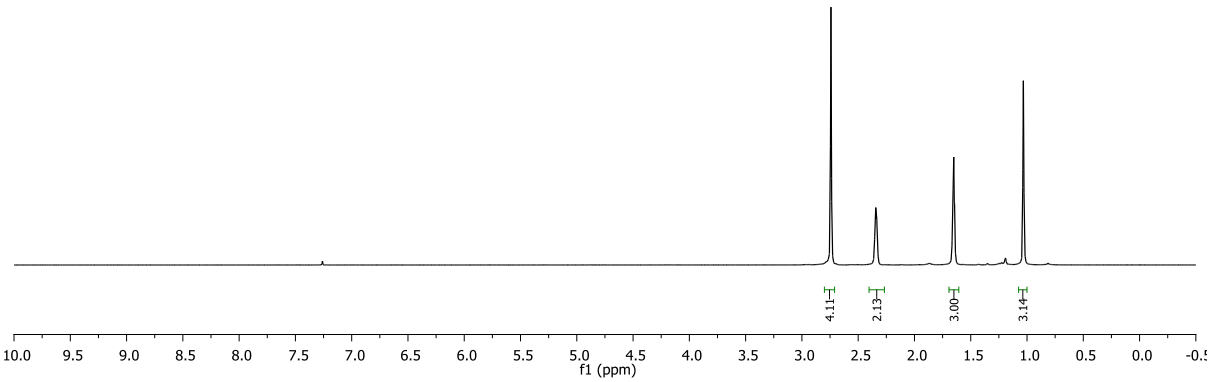


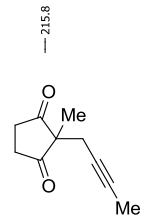
(^{13}C NMR, $CDCl_3$, 125 MHz)

2-(But-2-yn-1-yl)-2-methylcyclopentane-1,3-dione (2t):



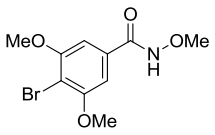
(^{1}H NMR, $CDCl_3$, 300 MHz)



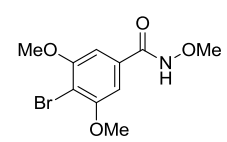


(^{13}C NMR, $CDCl_3$, 75 MHz)

4-Bromo-N,3,5-trimethoxybenzamide (1ac):

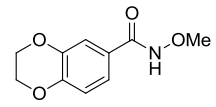


(**^{1}H NMR, $CDCl_3$, 500MHz**)

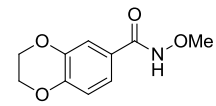


(**^{13}C NMR, $CDCl_3$+DMSO, 75 MHz**)

N-methoxy-2,3-dihydrobenzo[*b*][1,4]dioxine-6-carboxamide (1ad) :

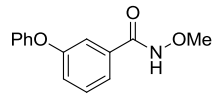


(^{1}H NMR, $CDCl_3$, 300 MHz)

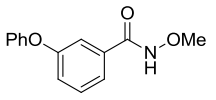


(^{13}C NMR, $CDCl_3$, 75 MHz)

N-Methoxy-3-phenoxybenzamide (1af) :

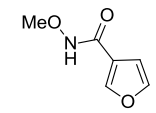


(**^{1}H NMR, $CDCl_3$, 500 MHz**)

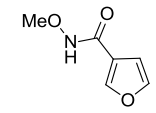


(**^{13}C NMR, $CDCl_3$, 75 MHz**)

N-Methoxyfuran-3-carboxamide (1ag) :

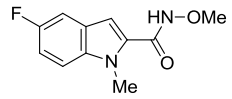


(¹H NMR, $CDCl_3$, 300 MHz)

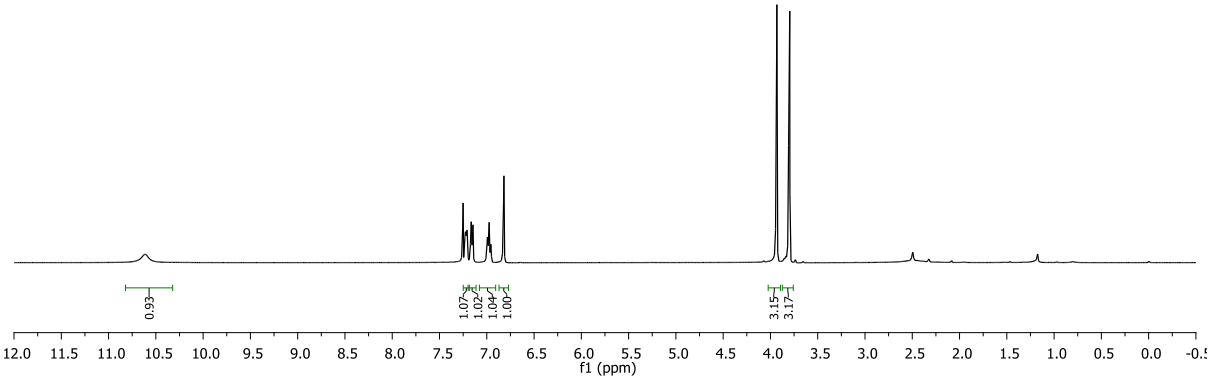


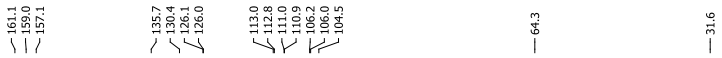
(¹³C NMR, $CDCl_3$, 75 MHz)

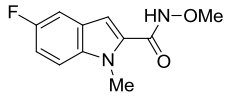
5-Fluoro-*N*-methoxy-1-methyl-1*H*-indole-2-carboxamide (1ah):



(**^{1}H NMR, $CDCl_3$, 500MHz**)

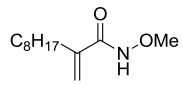




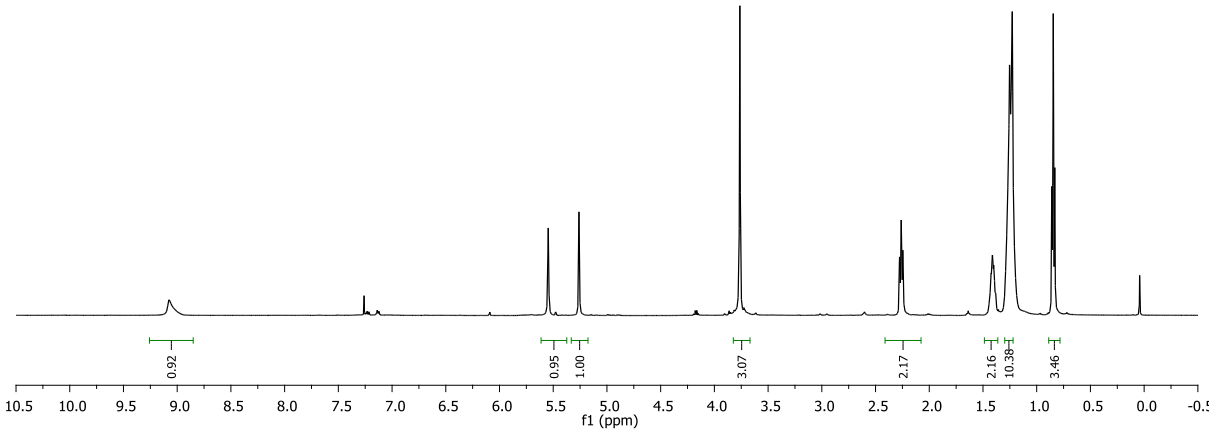


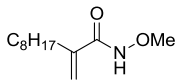
(**^{13}C NMR, $CDCl_3$, 125 MHz**)

N-Bethoxy-2-methylenedecanamide(1ak) :

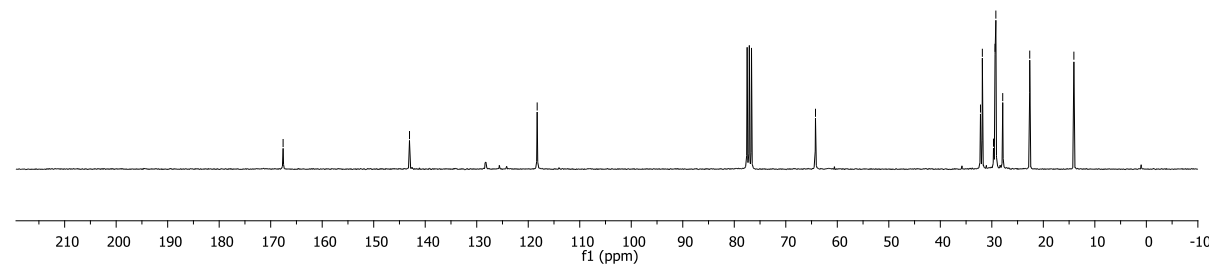


(**^{1}H NMR, $CDCl_3$, 500MHz**)

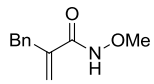




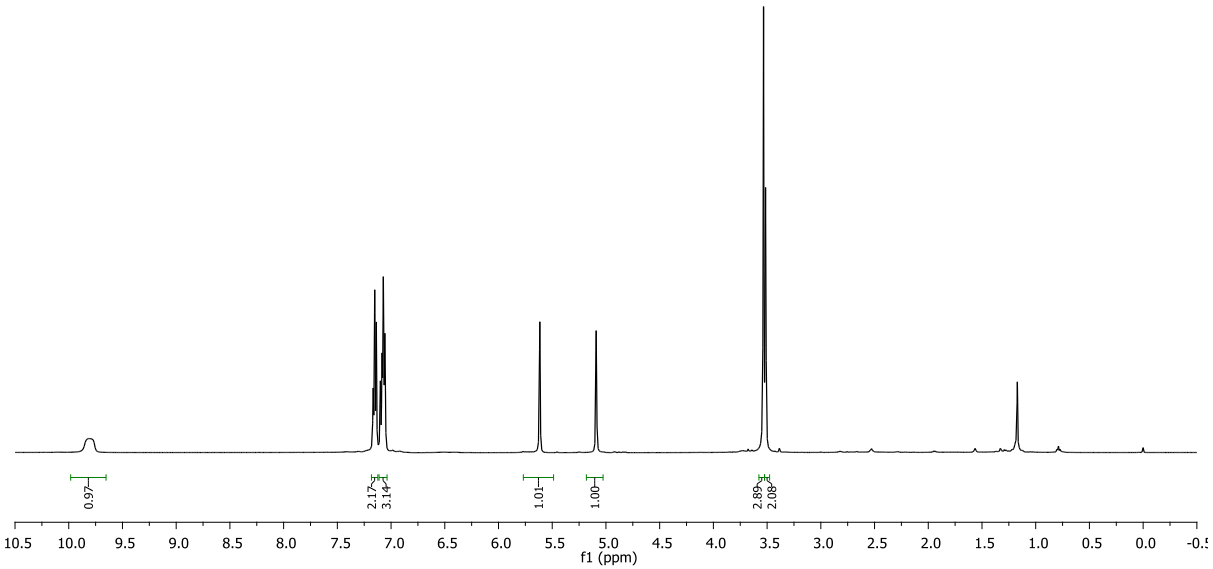
(**^{13}C NMR, $CDCl_3$, 75 MHz**)

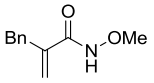


2-Benzyl-*N*-methoxyacrylamide (1am):



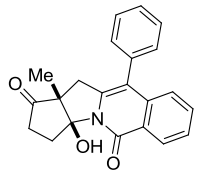
(^{1}H NMR, $CDCl_3$, 500 MHz)



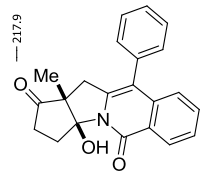


(^{13}C NMR, $CDCl_3$, 125 MHz)

3a-Hydroxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3a):

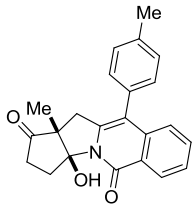


(^{1}H NMR, $CDCl_3$, 400MHz)

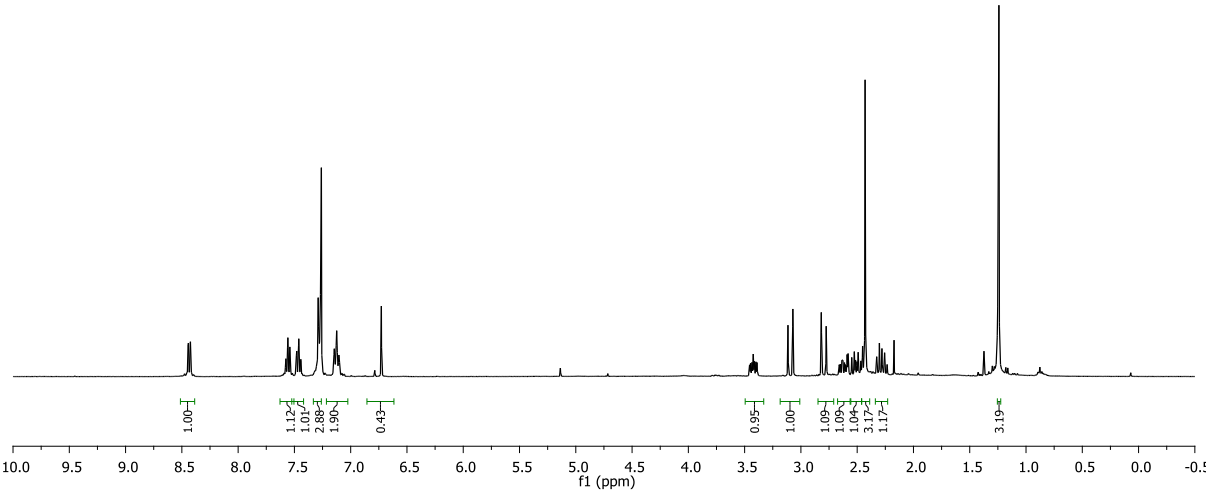


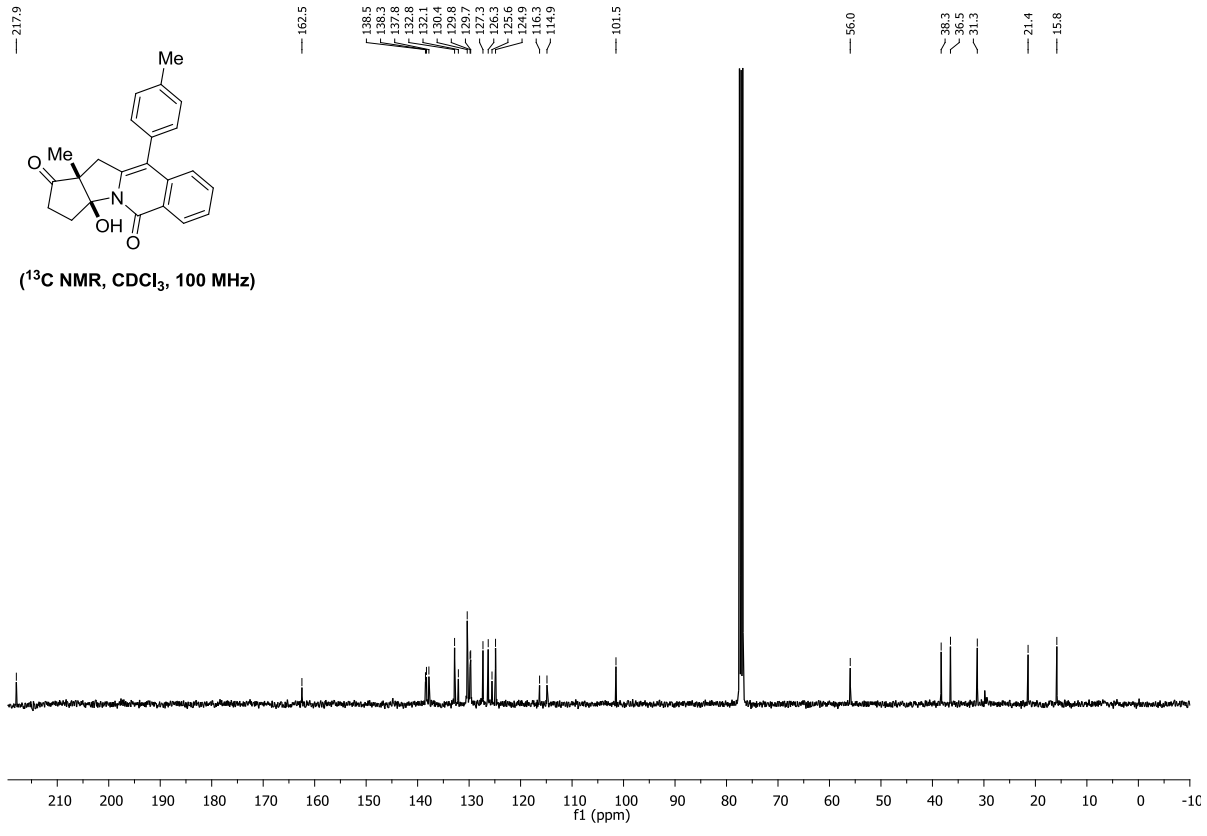
(^{13}C NMR, $CDCl_3$, 75MHz)

3a-Hydroxy-11a-methyl-10-(*p*-tolyl)-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3b):



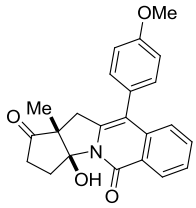
(^{1}H NMR, $CDCl_3$, 400 MHz)



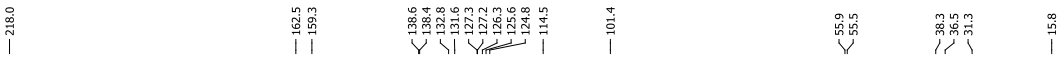


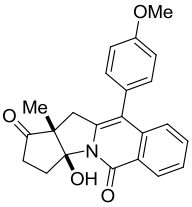
(^{13}C NMR, $CDCl_3$, 100 MHz)

3a-Hydroxy-10-(4-methoxyphenyl)-11a-methyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3c):

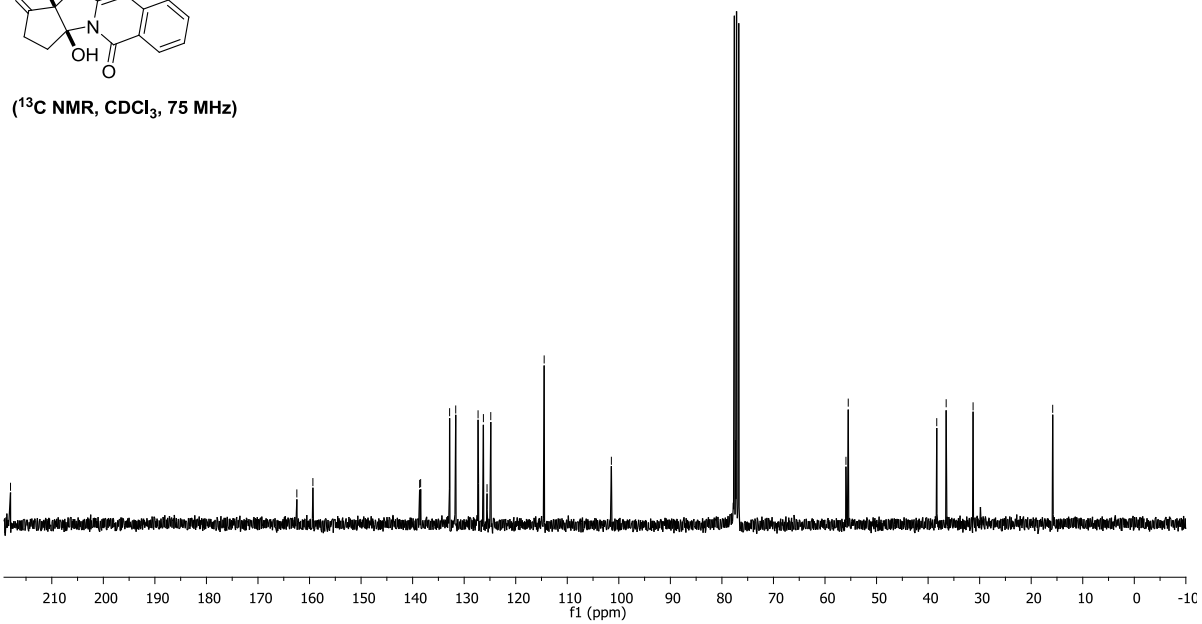


(¹H NMR, $CDCl_3$, 500 MHz)

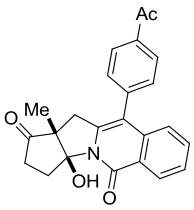




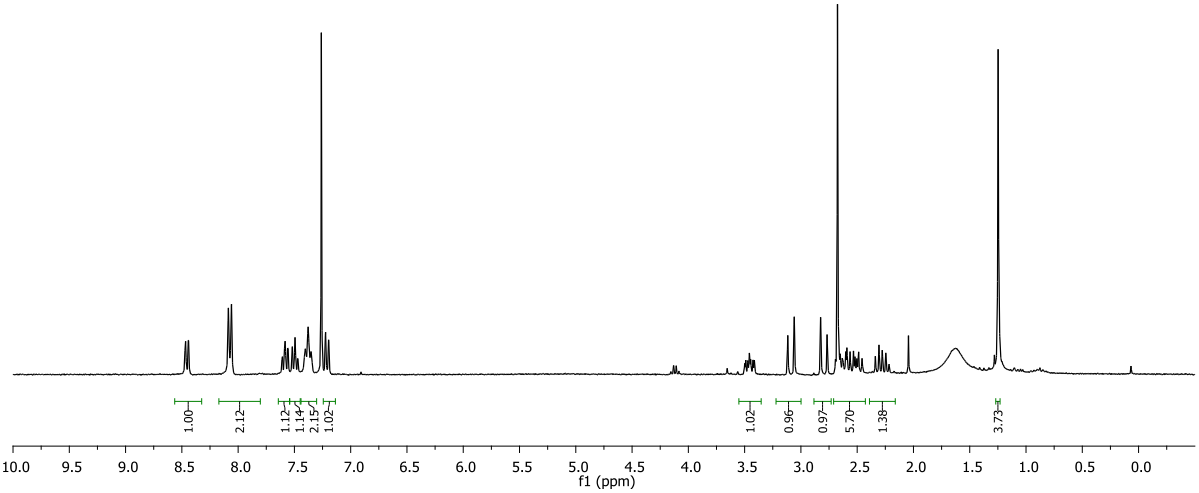
(¹³C NMR, $CDCl_3$, 75 MHz)

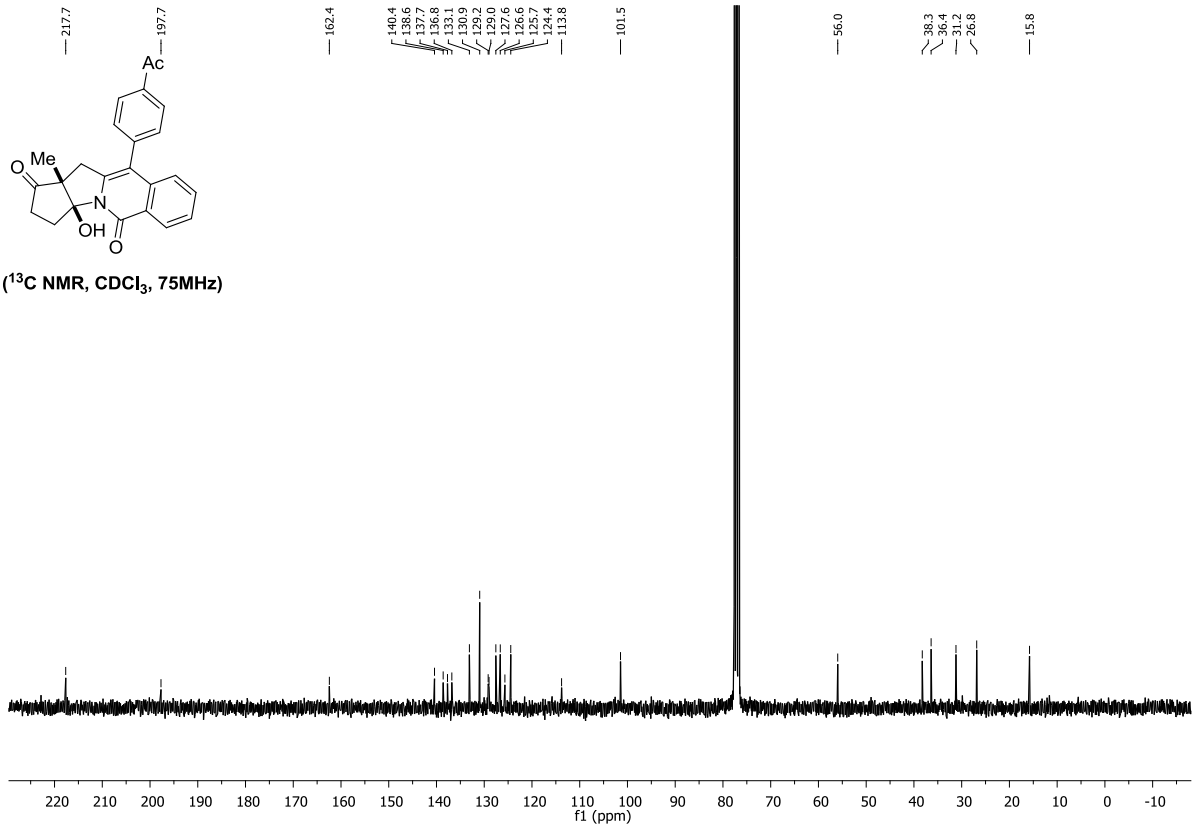


10-(4-Acetylphenyl)-3a-hydroxy-11a-methyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3d):



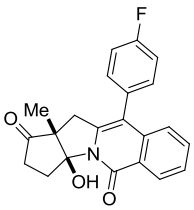
(¹H NMR, $CDCl_3$, 300MHz)



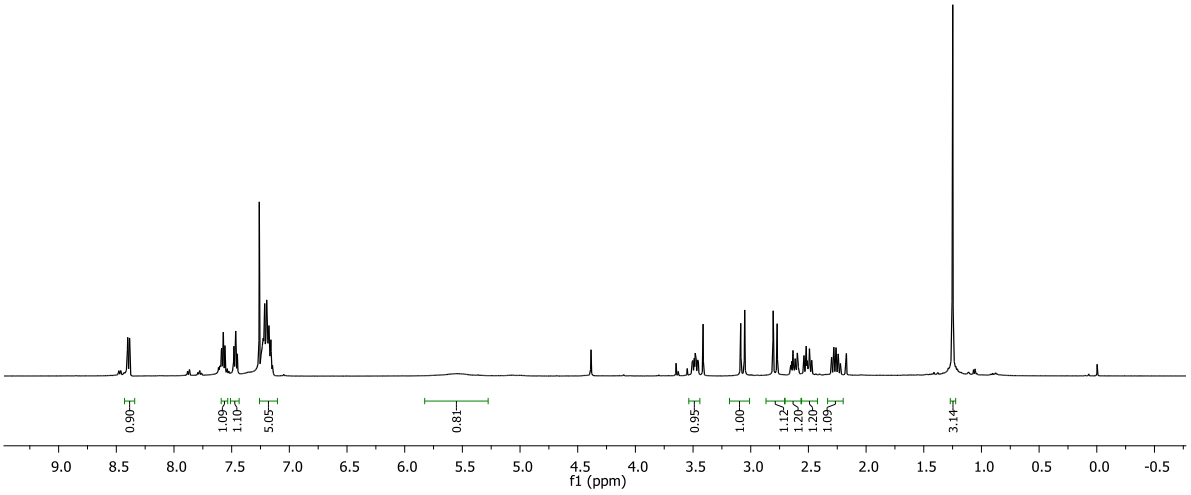


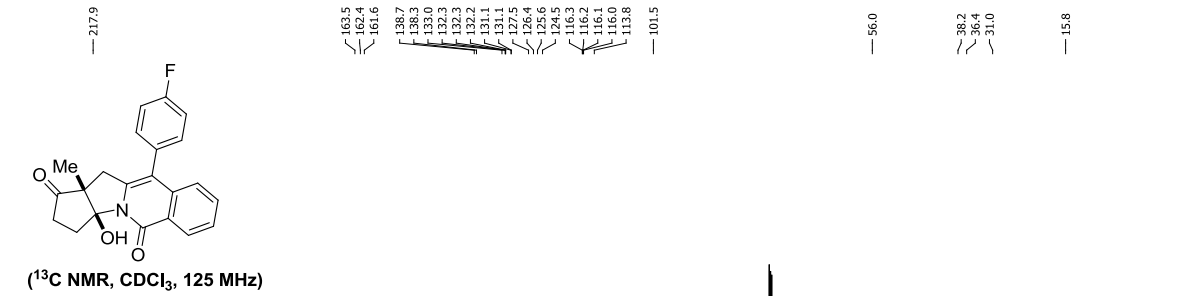
(¹³C NMR, $CDCl_3$, 75MHz)

10-(4-Fluorophenyl)-3a-hydroxy-11a-methyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3e):

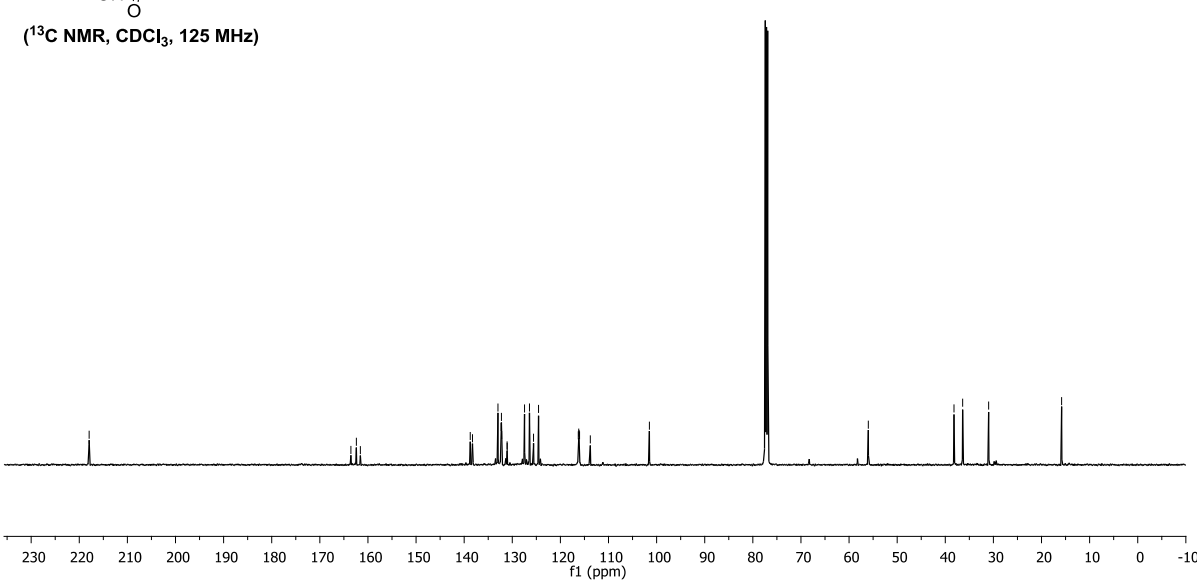


(¹H NMR, $CDCl_3$, 500 MHz)

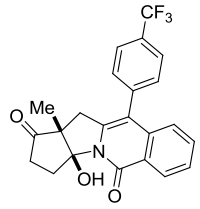




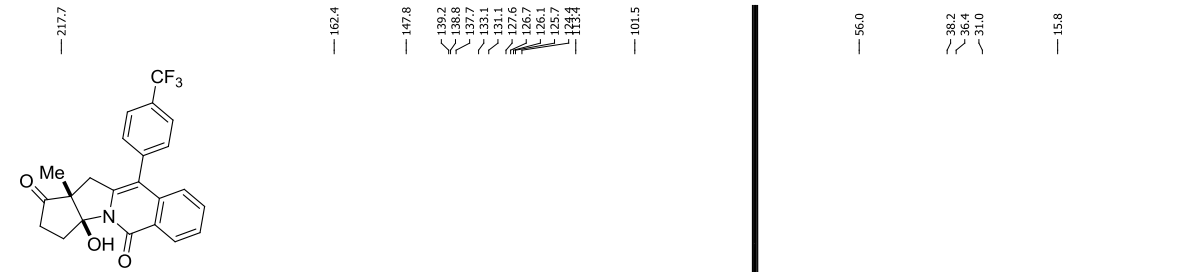
(¹³C NMR, $CDCl_3$, 125 MHz)



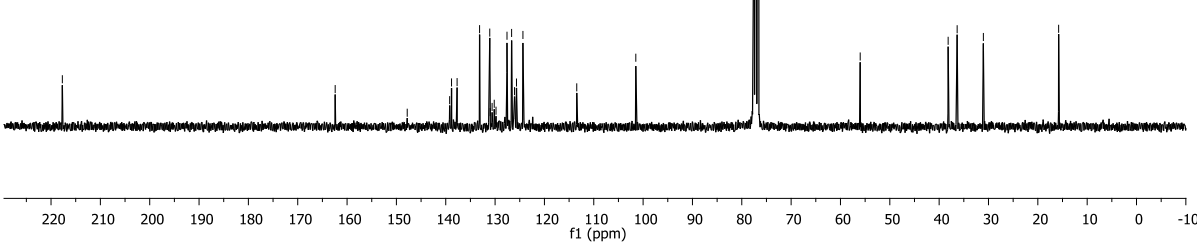
3a-Hydroxy-11a-methyl-10-(4-(trifluoromethyl)phenyl)-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3f):



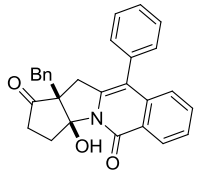
(¹H NMR, $CDCl_3$, 500 MHz)



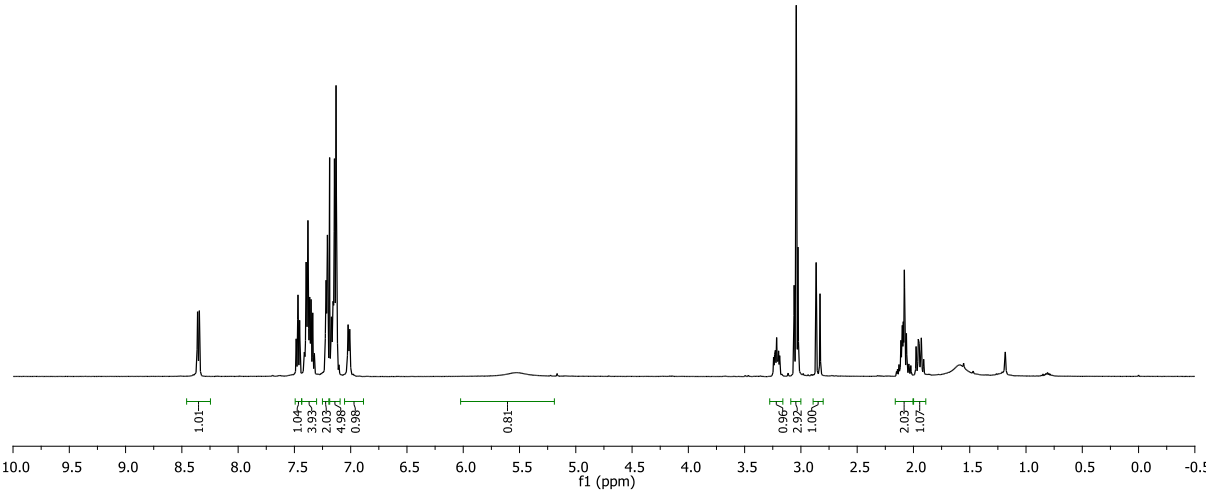
(¹³C NMR, $CDCl_3$, 75 MHz)

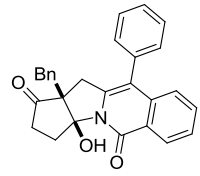


11a-Benzyl-3a-hydroxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3g):



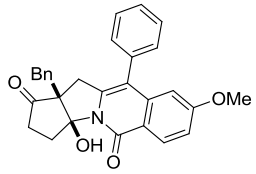
(^{1}H NMR, $CDCl_3$, 500MHz)



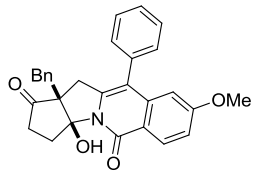


(^{13}C NMR, $CDCl_3$, 125MHz)

11a-Benzyl-3a-hydroxy-8-methoxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3h):

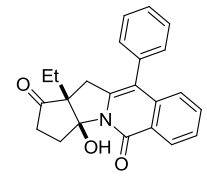


(^{1}H NMR, $CDCl_3$, 500 MHz)

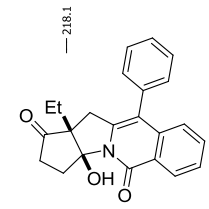


(^{13}C NMR, $CDCl_3$, 75 MHz)

11a-Ethyl-3a-hydroxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3i):

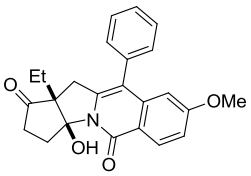


(¹H NMR, $CDCl_3$, 500 MHz)

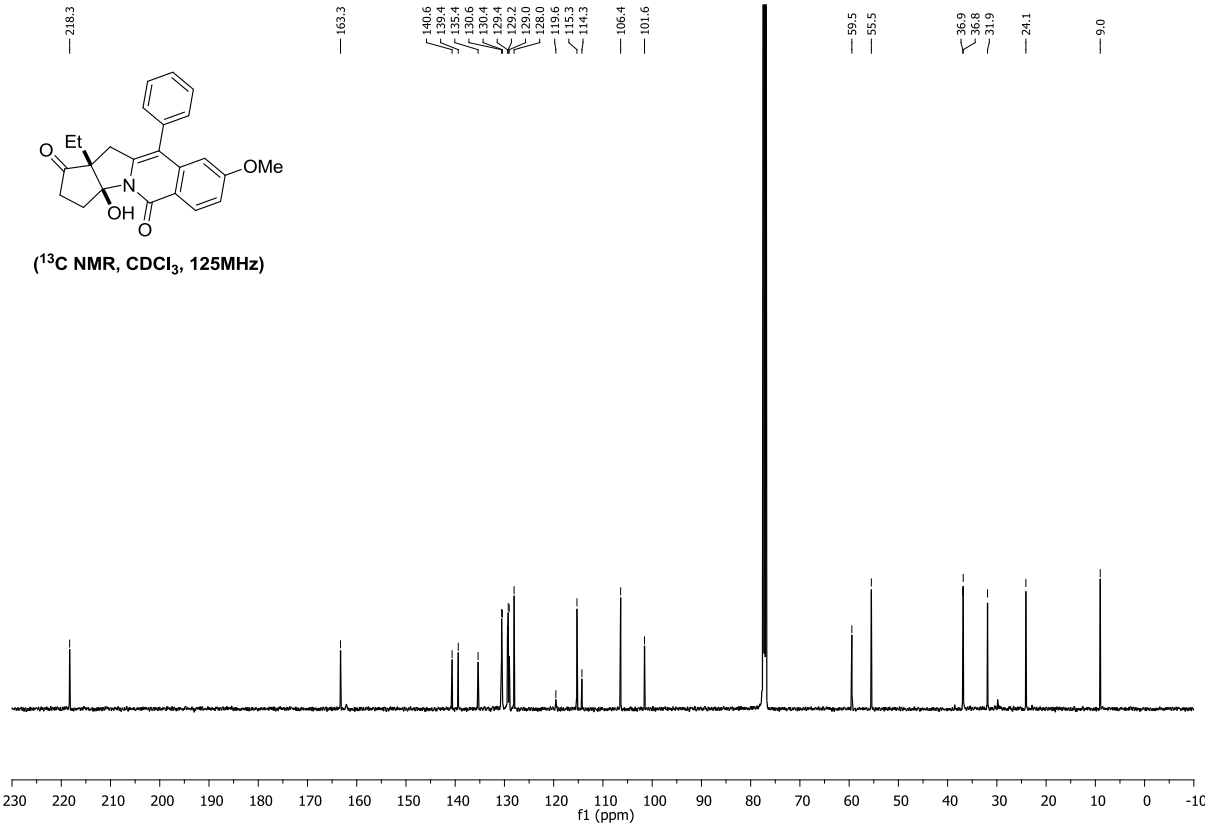


(¹³C NMR, $CDCl_3$, 125 MHz)

11a-Ethyl-3a-hydroxy-8-methoxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3j):

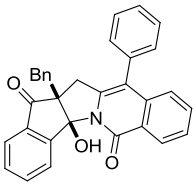


(^{1}H NMR, $CDCl_3$, 500MHz)

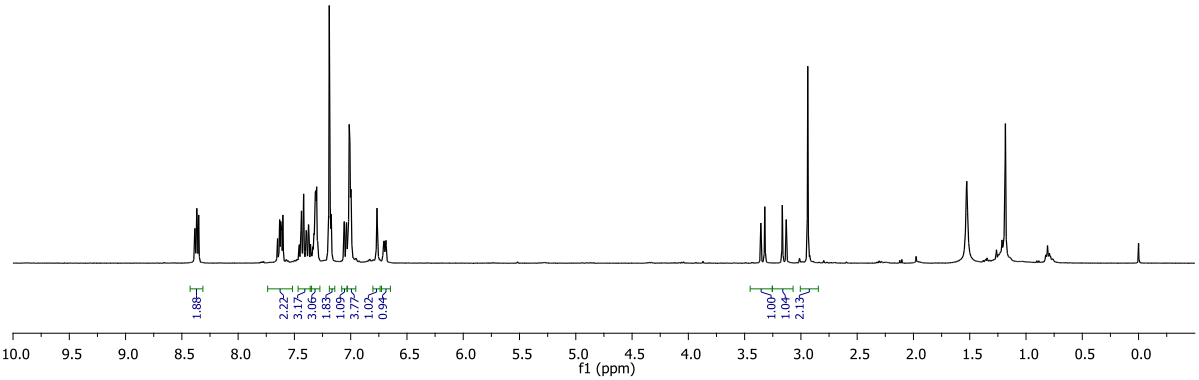


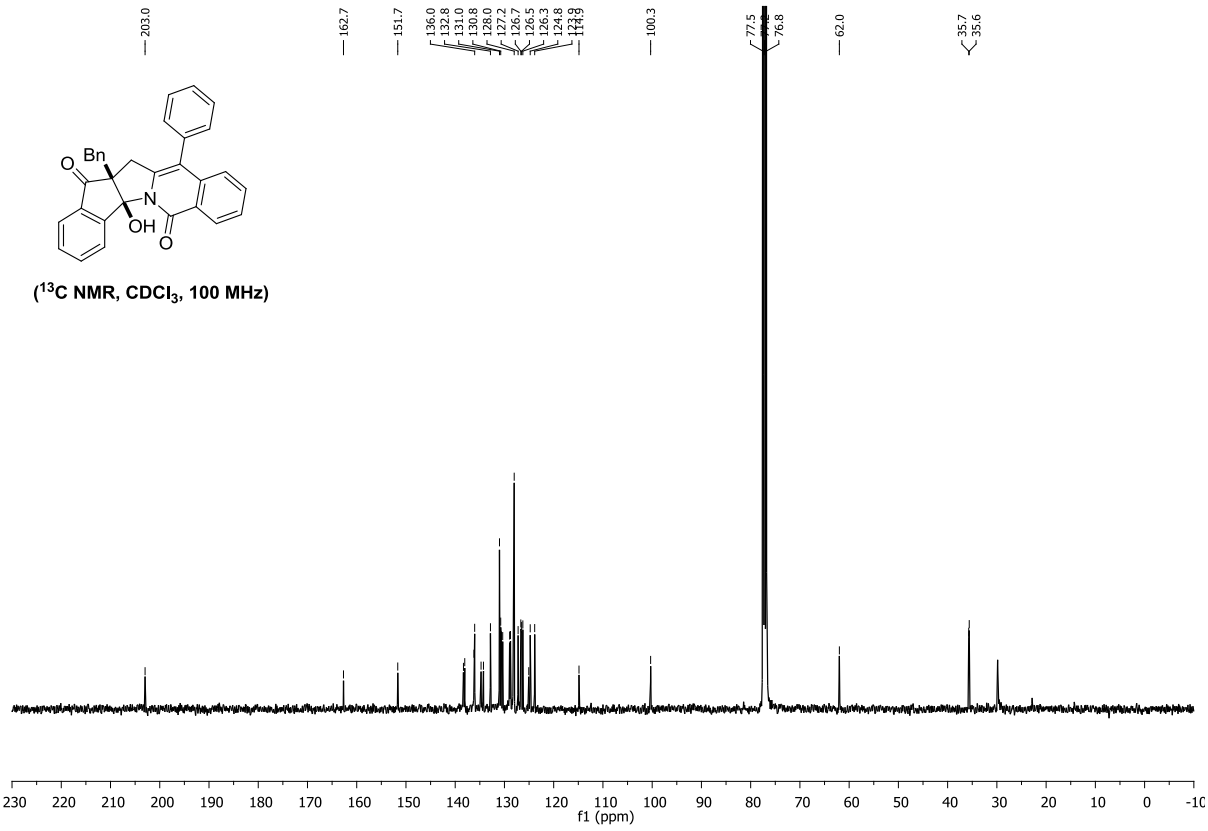
(^{13}C NMR, $CDCl_3$, 125MHz)

12a-Benzyl-4b-hydroxy-11-phenyl-12,12a-dihydro-4b*H*-indeno[2',1':4,5]pyrrolo[1,2-*b*]isoquinoline-6,13-dione (3k):



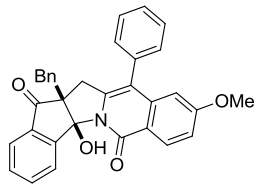
(^{1}H NMR, $CDCl_3$, 400 MHz)



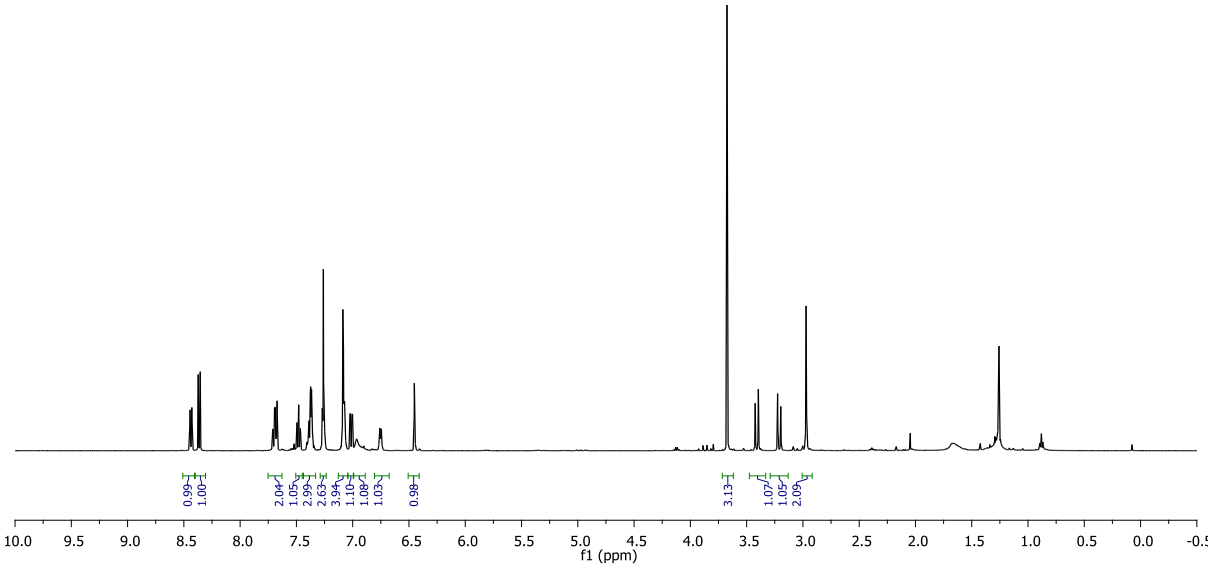


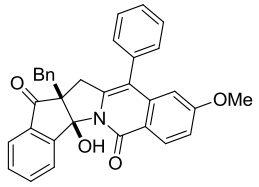
(^{13}C NMR, $CDCl_3$, 100 MHz)

12a-Benzyl-4b-hydroxy-9-methoxy-11-phenyl-12,12a-dihydro-4b*H*-indeno[2',1':4,5]pyrrolo[1,2-*b*]isoquinoline-6,13-dione (3l):



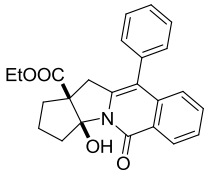
(^{1}H NMR, $CDCl_3$, 500 MHz)



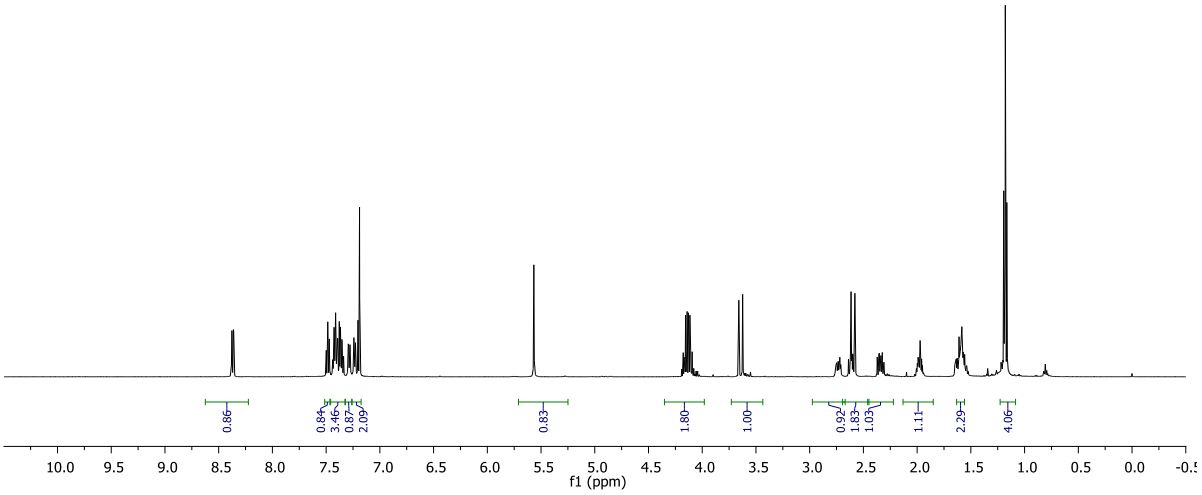


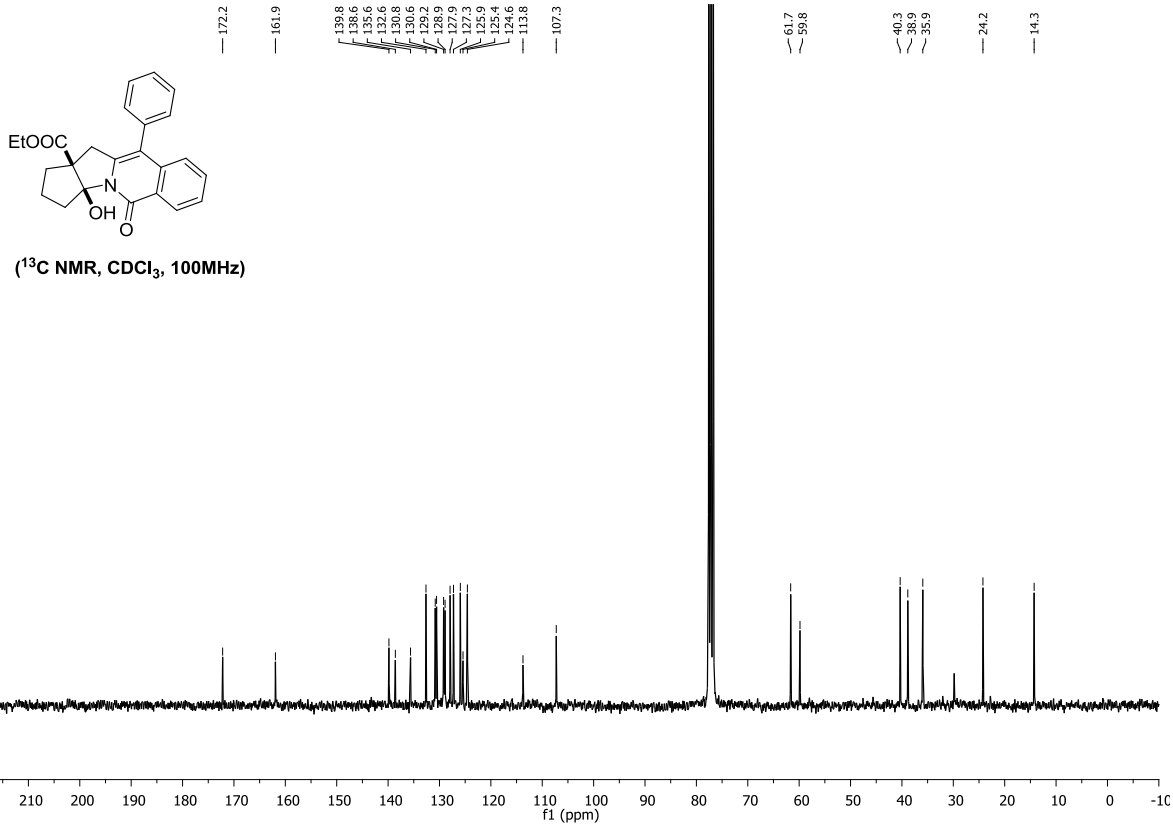
(^{13}C NMR, $CDCl_3$, 125 MHz)

Ethyl 3a-hydroxy-5-oxo-10-phenyl-2,3,3a,5,11,11a-hexahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-11a-carboxylate (3m):



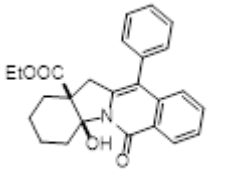
(¹H NMR, $CDCl_3$, 500MHz)



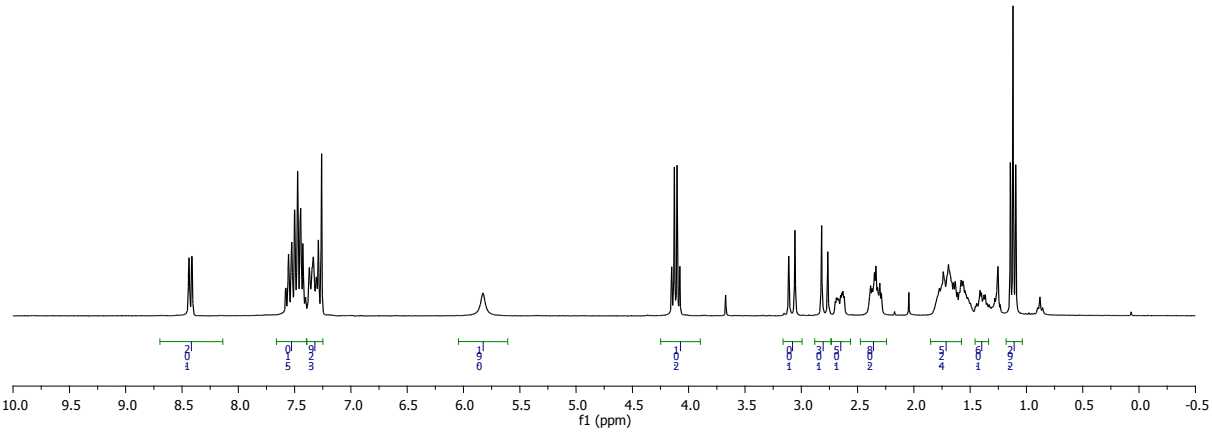


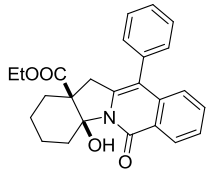
(¹³C NMR, $CDCl_3$, 100MHz)

Ethyl 4a-hydroxy-6-oxo-11-phenyl-1,2,3,4,4a,6,12,12a-octahydroindolo[1,2-*b*]isoquinoline-12a-carboxylate (3n):



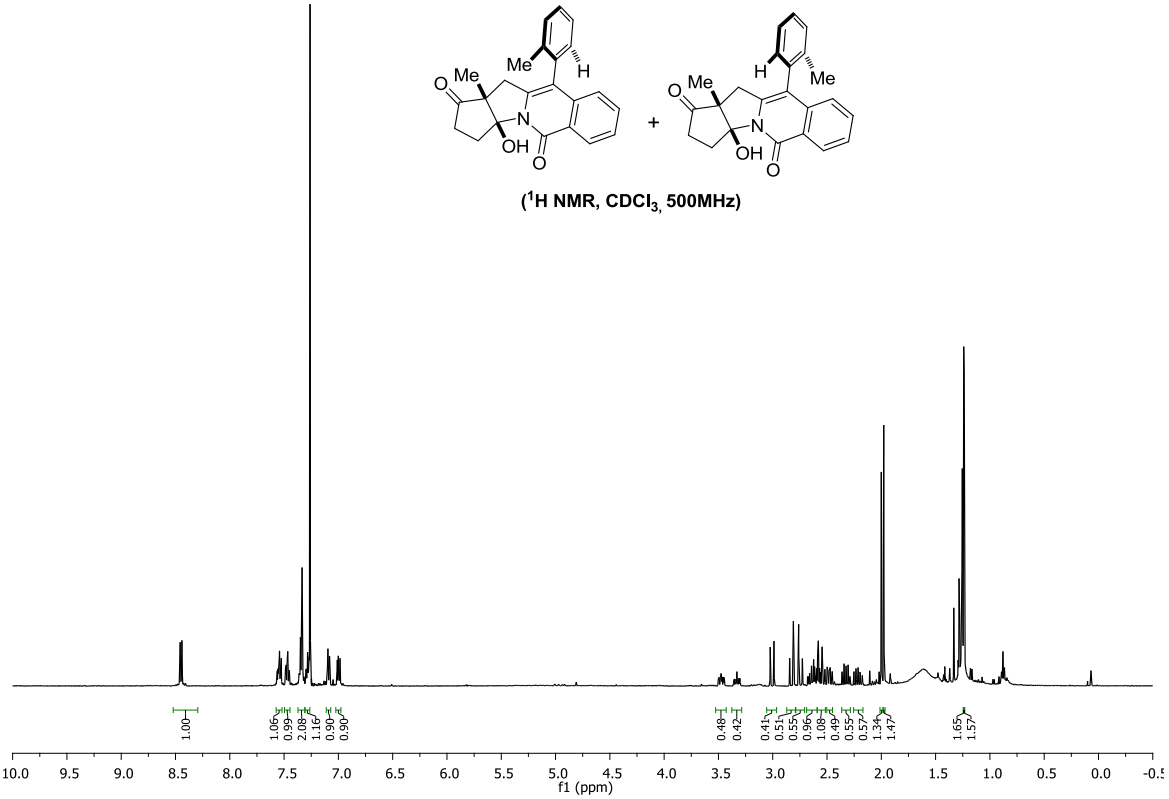
(^{1}H NMR, $CDCl_3$, 300 MHz)

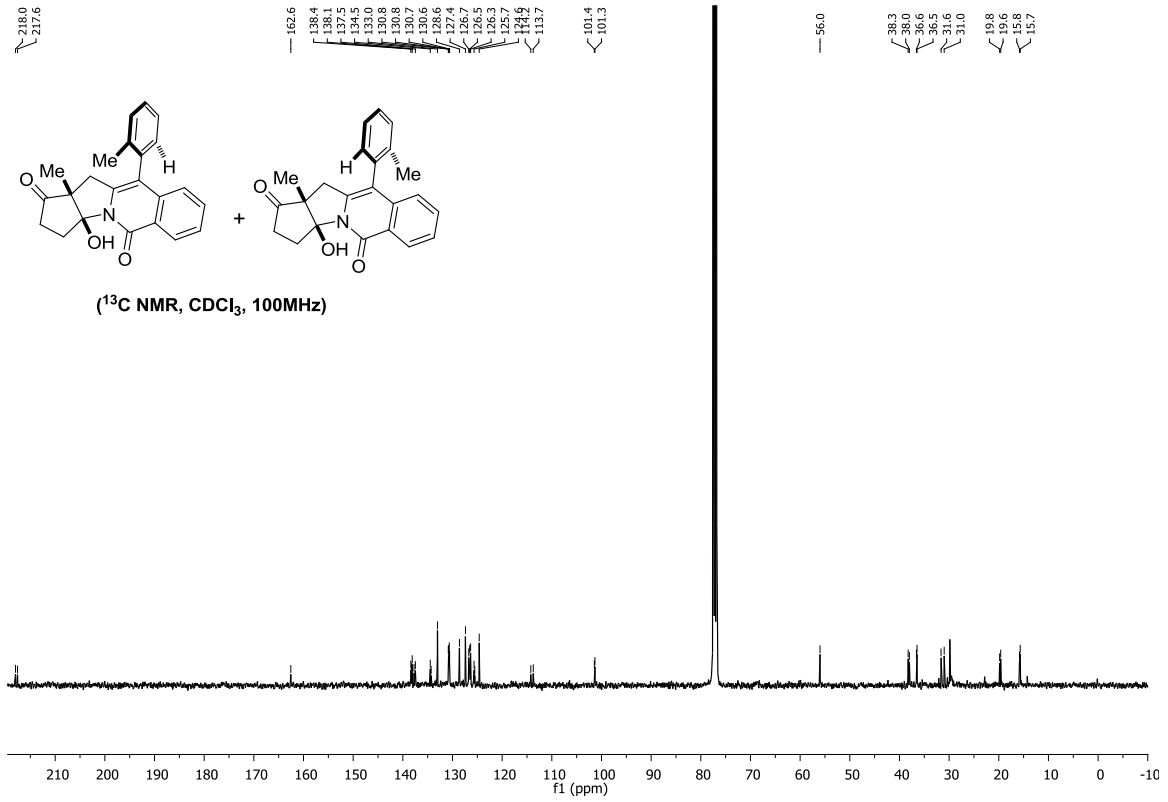




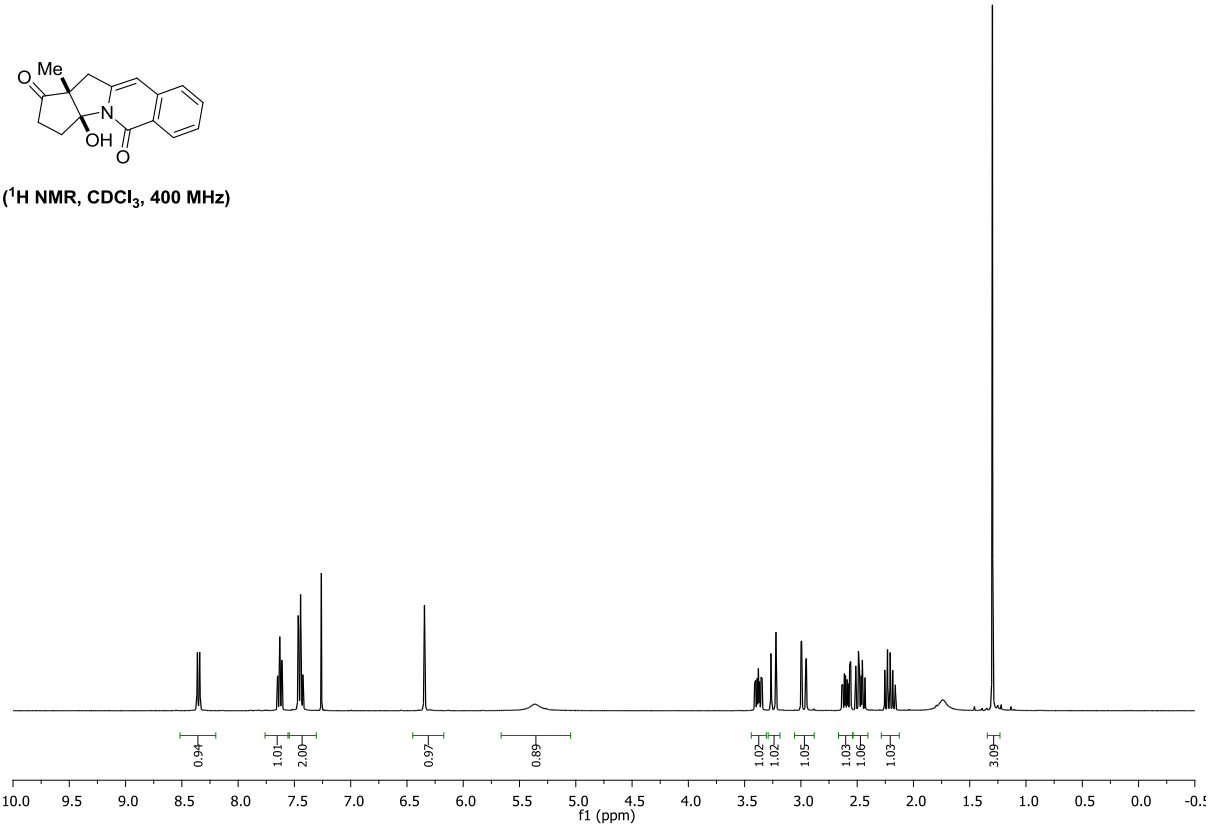
(^{13}C NMR, $CDCl_3$, 75 MHz)

3a-Hydroxy-11a-methyl-10-(*o*-tolyl)-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione(3o&3o[1]; mixture of atropisomers:

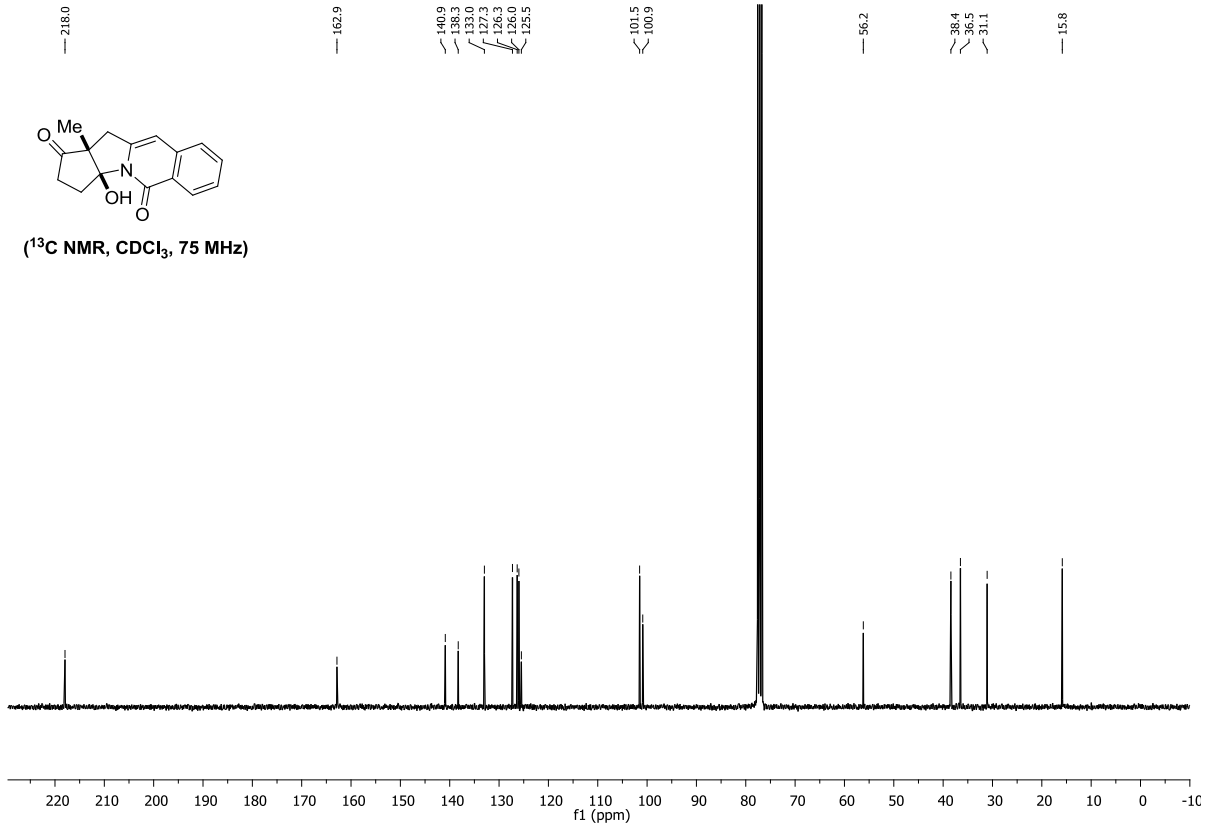




3a-Hydroxy-11a-methyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-b]isoquinoline-1,5(2*H*)-dione (3p):

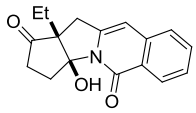


(^{1}H NMR, $CDCl_3$, 400 MHz)

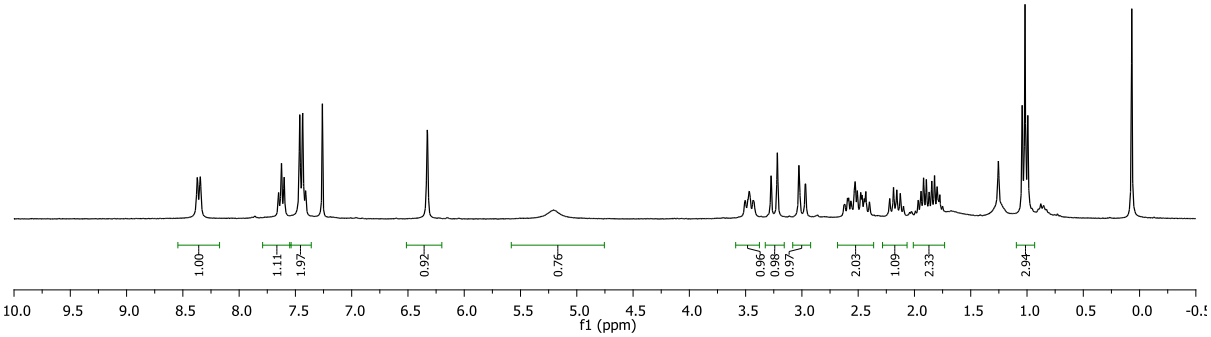


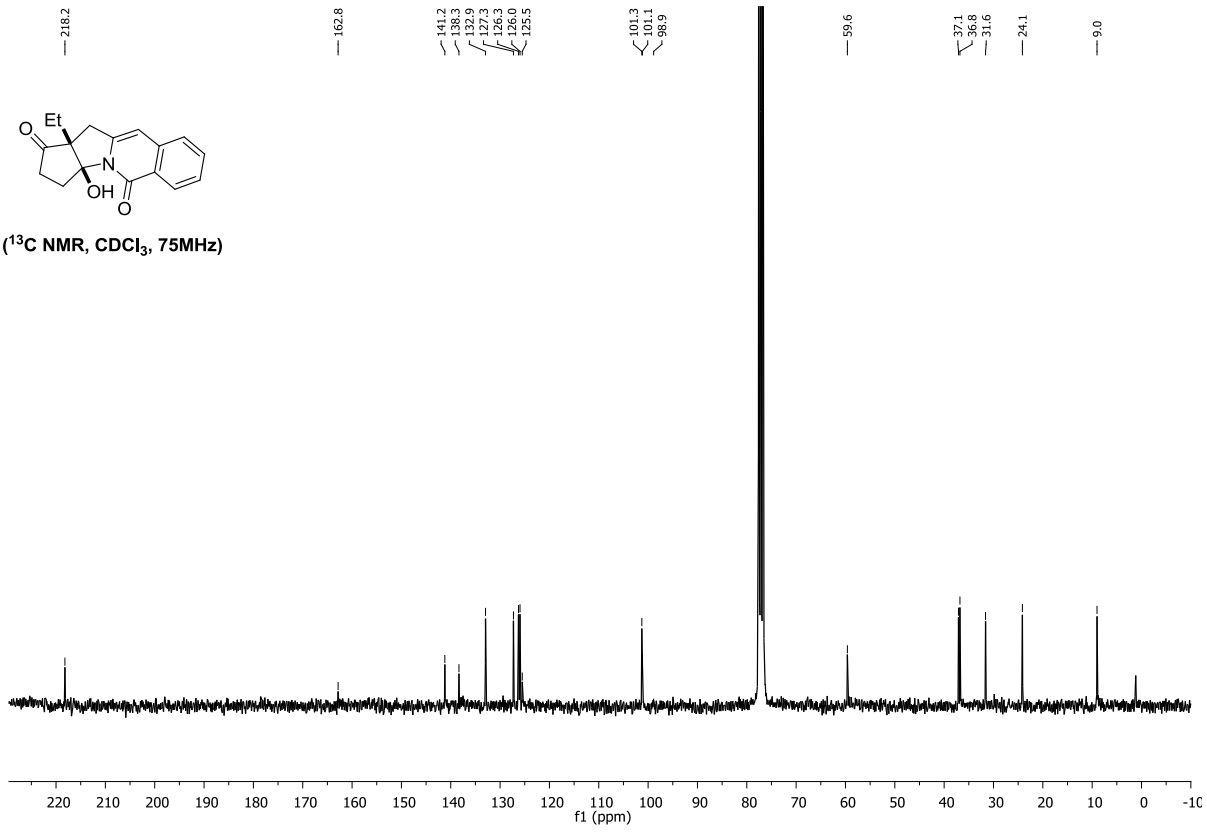
(^{13}C NMR, $CDCl_3$, 75 MHz)

11a-Ethyl-3a-hydroxy-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3q)



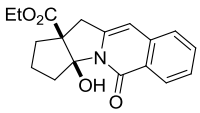
(^{1}H NMR, $CDCl_3$, 300MHz)



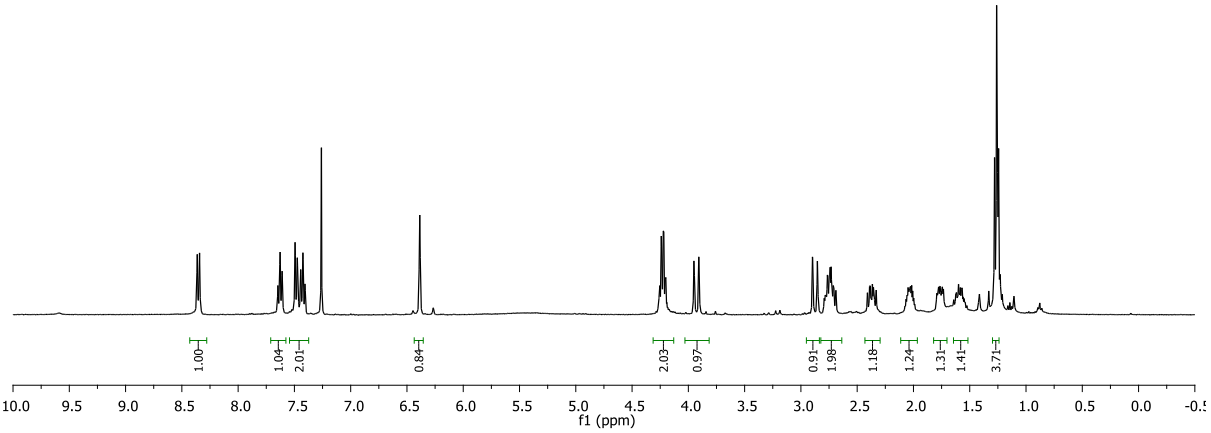


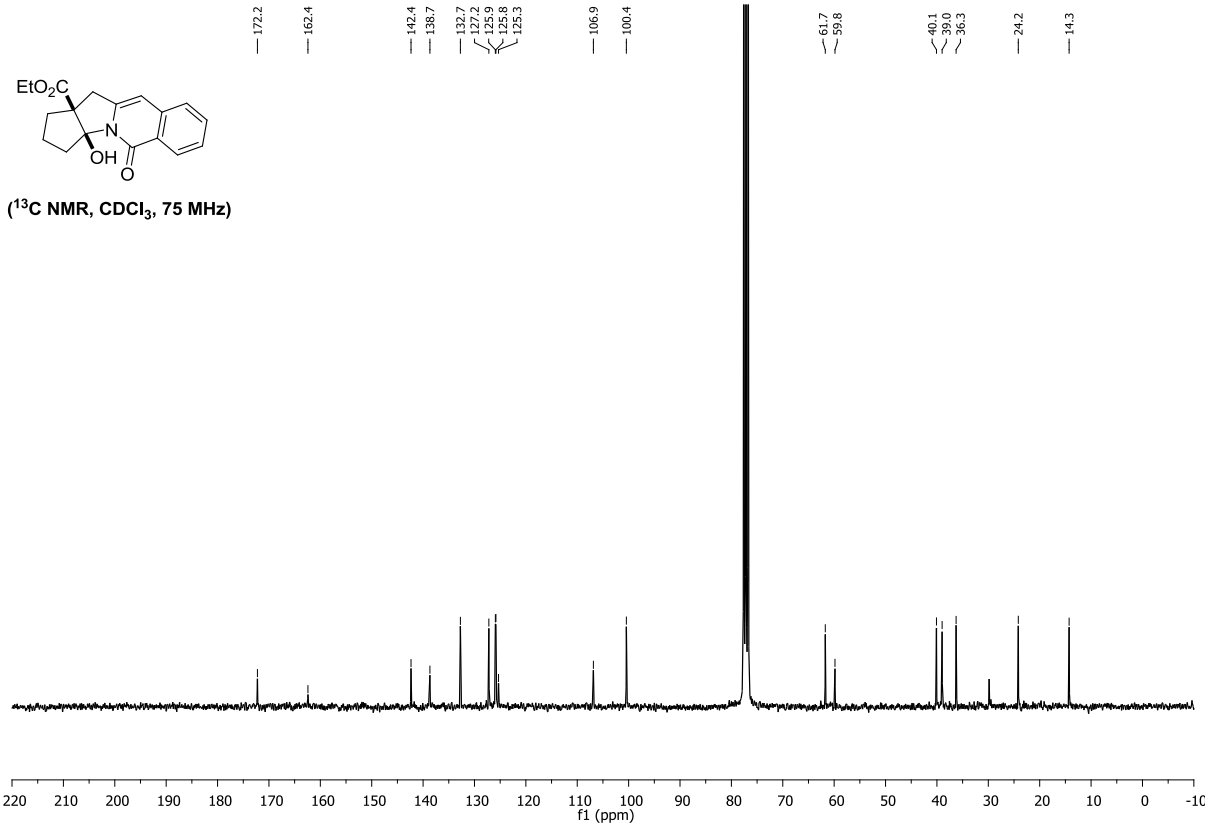
(^{13}C NMR, $CDCl_3$, 75MHz)

Ethyl 3a-hydroxy-5-oxo-2,3,3a,5,11,11a-hexahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-11a-carboxylate (3r):



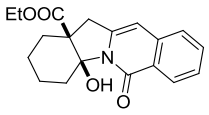
(**^{1}H NMR, $CDCl_3$, 400 MHz**)



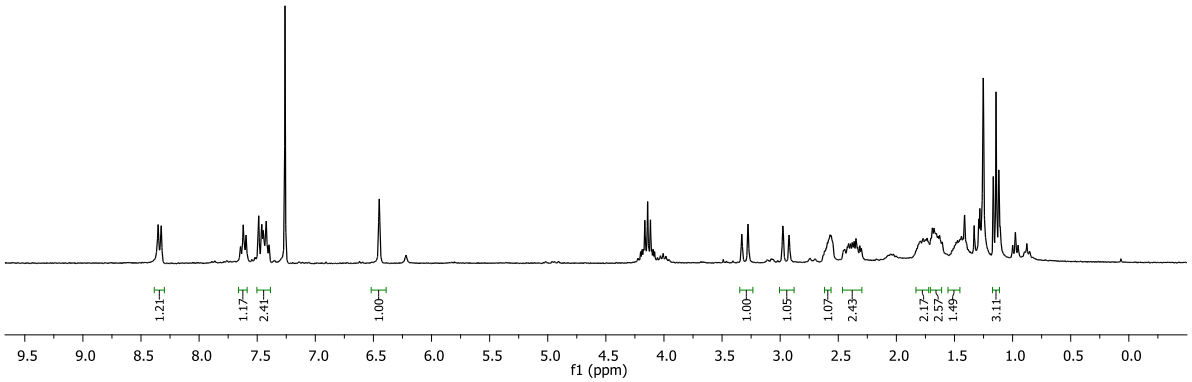


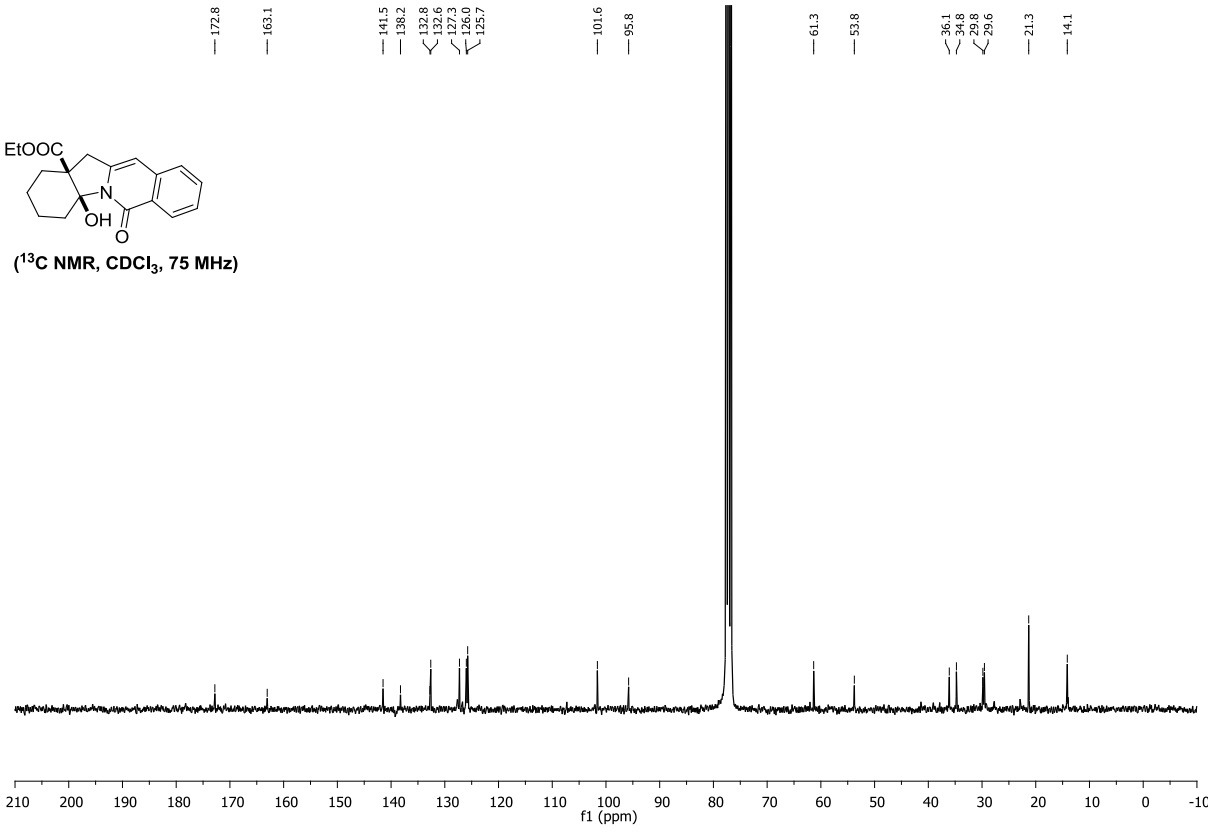
(**^{13}C NMR, $CDCl_3$, 75 MHz**)

Ethyl 4a-hydroxy-6-oxo-1,2,3,4,4a,6,12,12a-octahydroindolo[1,2-*b*]isoquinoline-12a-carboxylate (3s):



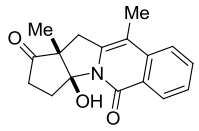
(^{1}H NMR, $CDCl_3$, 300 MHz)



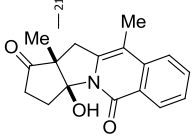


(^{13}C NMR, $CDCl_3$, 75 MHz)

3a-Hydroxy-10,11a-dimethyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3t):

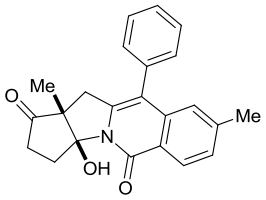


(**^{1}H NMR, $CDCl_3$, 300 MHz**)

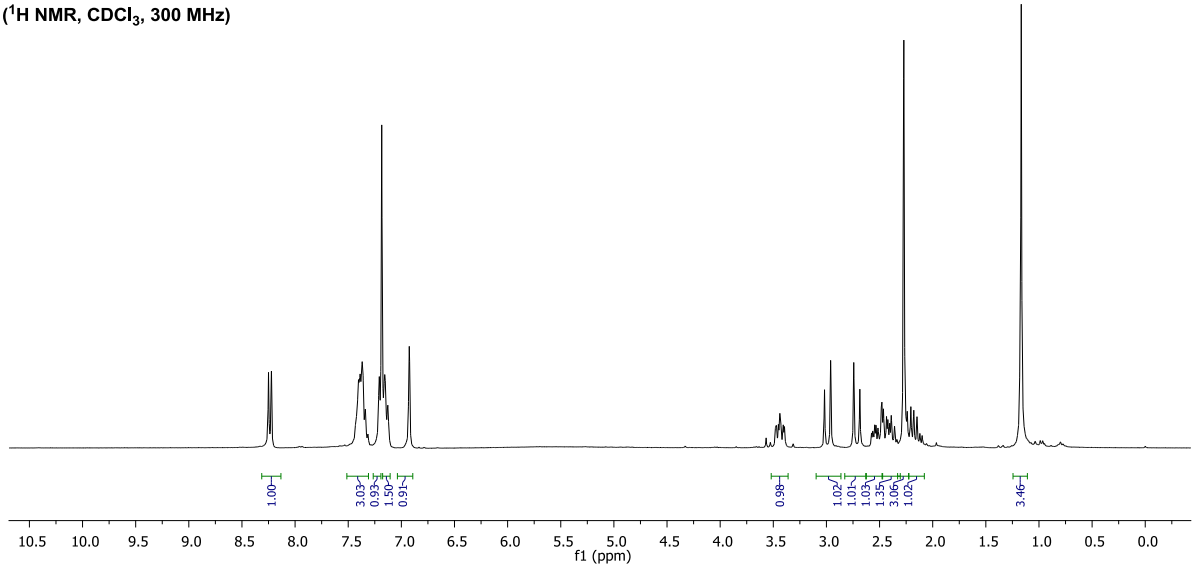


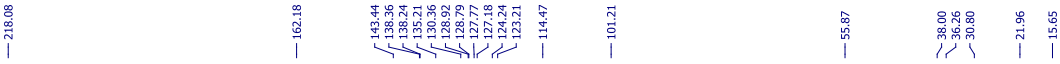
(**^{13}C NMR, $CDCl_3$, 75 MHz**)

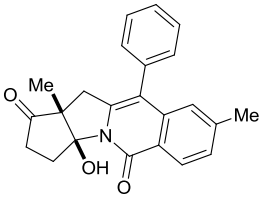
3a-Hydroxy-8,11a-dimethyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3u) :



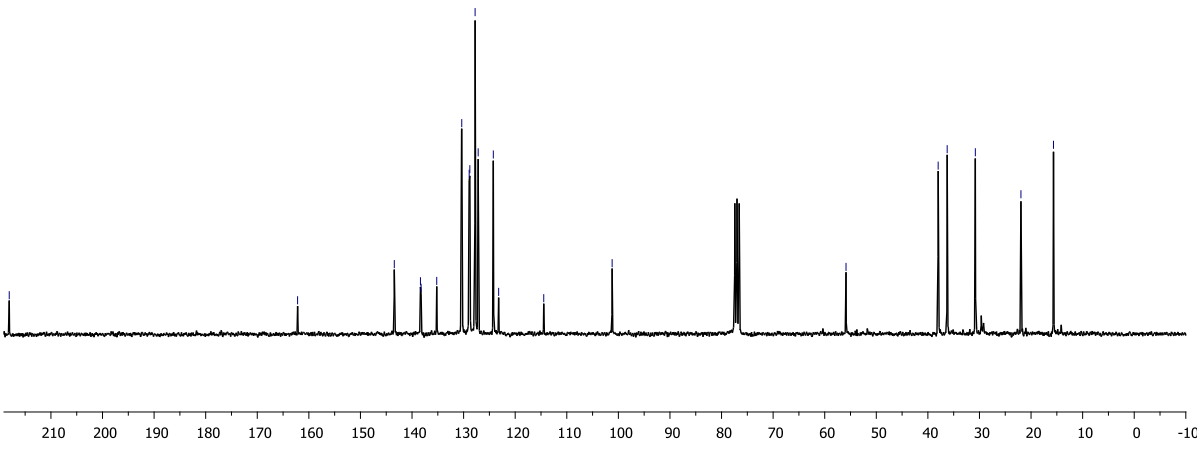
(¹H NMR, $CDCl_3$, 300 MHz)



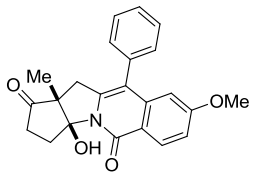




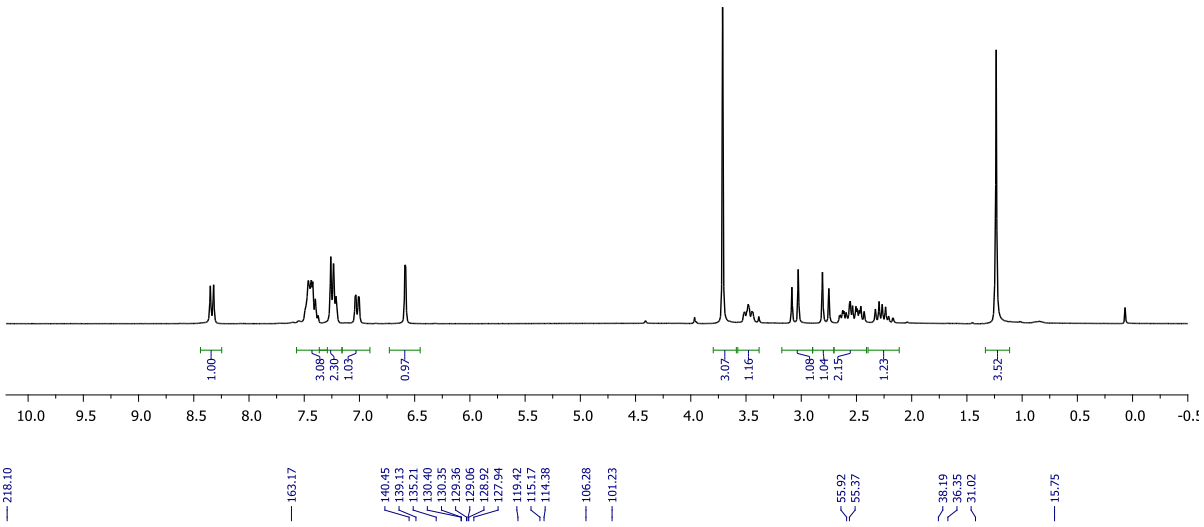
(¹³C NMR, $CDCl_3$, 75 MHz)

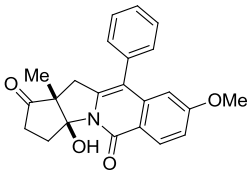


3a-Hydroxy-8-methoxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3v):

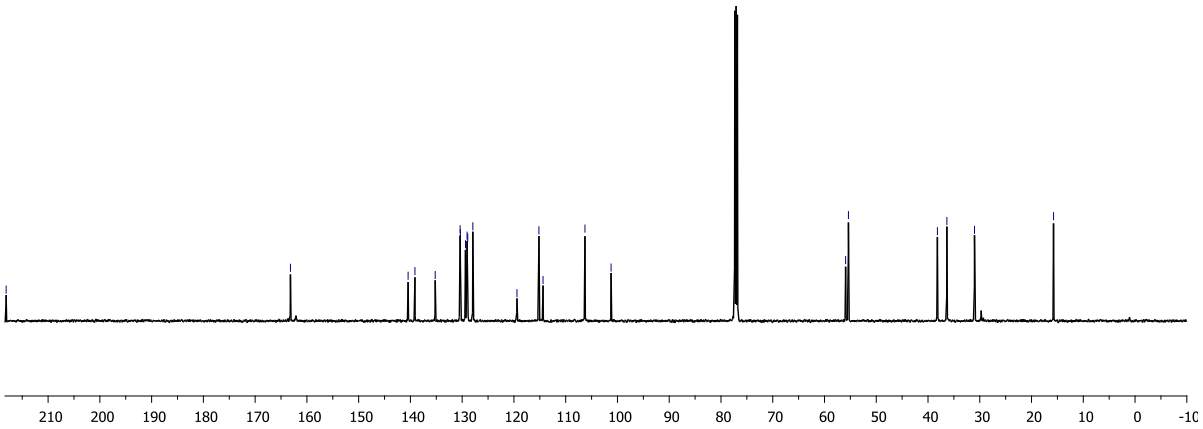


(^{1}H NMR, $CDCl_3$, 300 MHz)

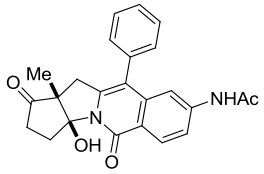




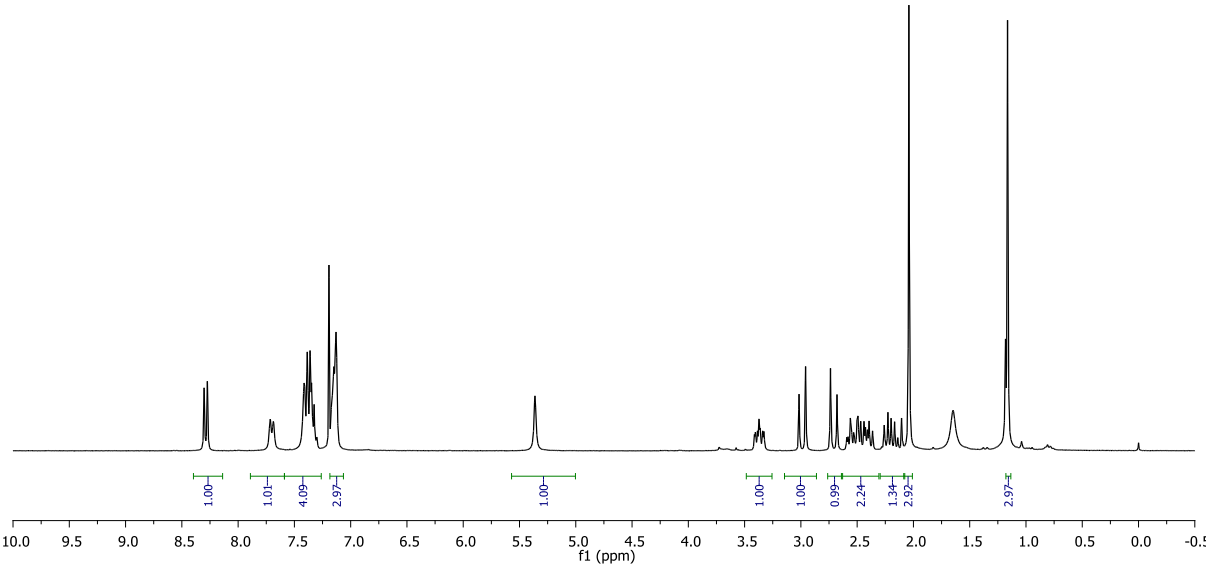
(^{13}C NMR, $CDCl_3$, 125 MHz)

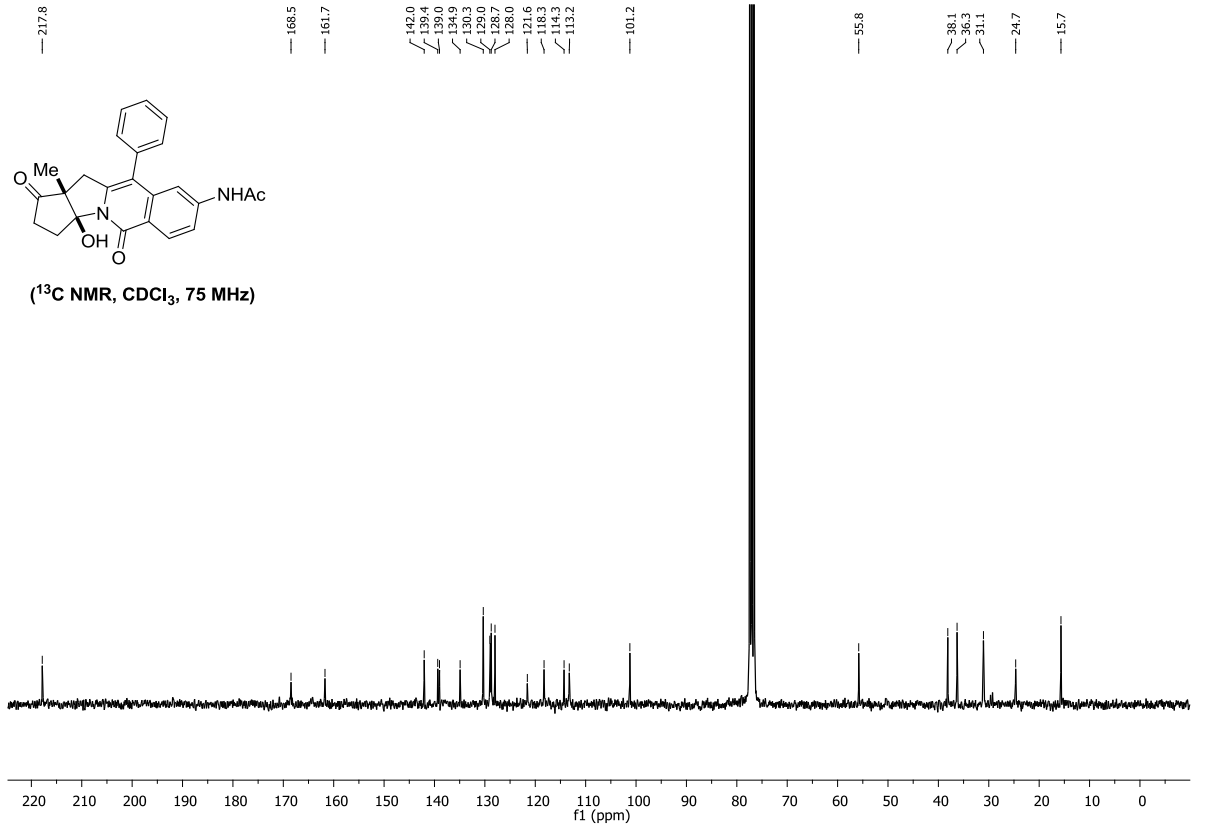


_N_-(3a-Hydroxy-11a-methyl-1,5-dioxo-10-phenyl-2,3,3a,5,11,11a-hexahydro-1_H_-cyclopenta[4,5]pyrrolo[1,2-_b_]isoquinolin-8-yl)acetamide (3w) :



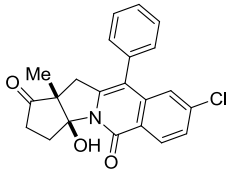
(**^{1}H NMR, $CDCl_3$, 300 MHz**)



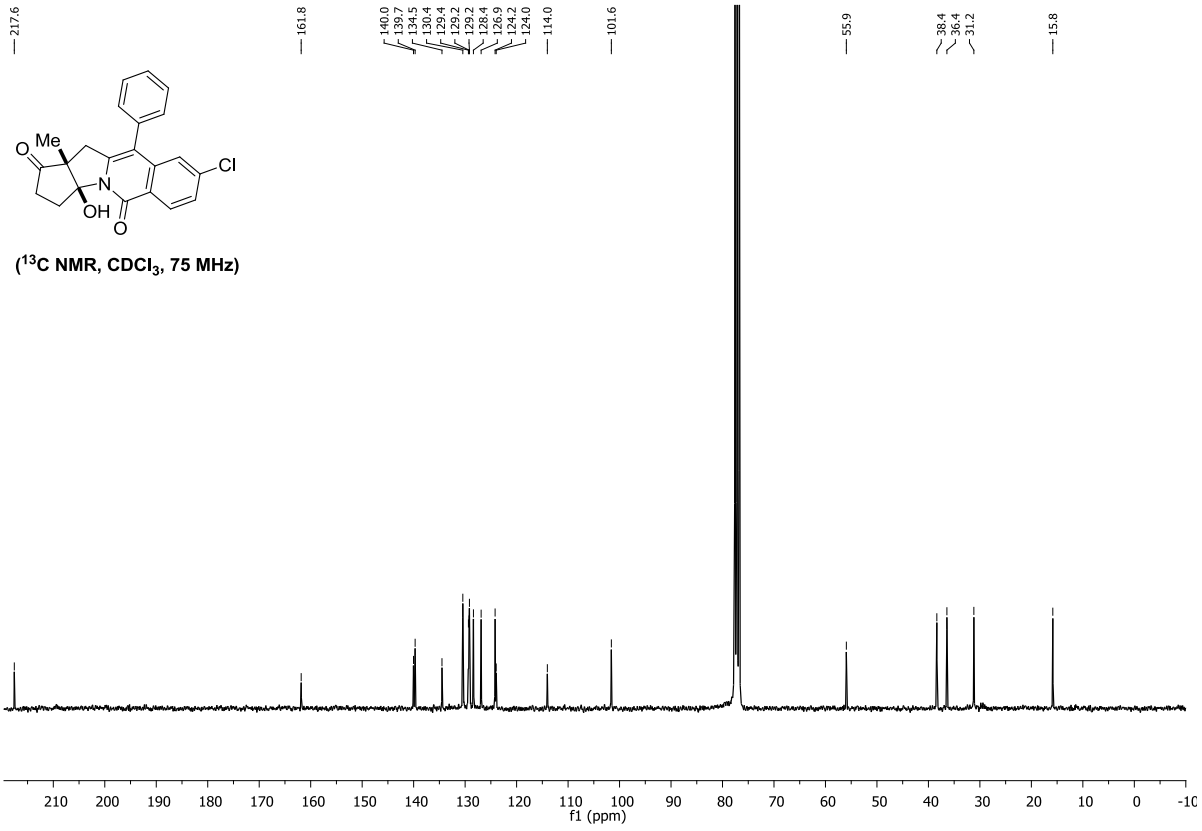


(**^{13}C NMR, $CDCl_3$, 75 MHz**)

8-Chloro-3a-hydroxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3x):

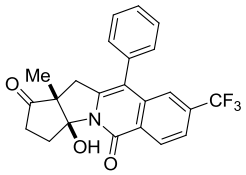


(**^{1}H NMR, $CDCl_3$, 300 MHz**)

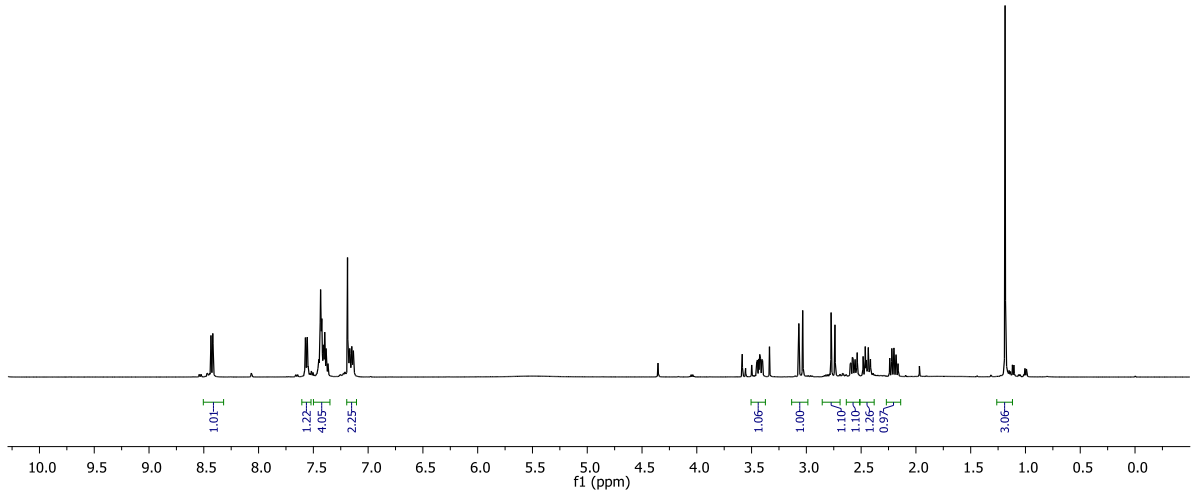


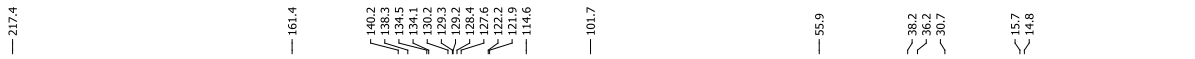
(**^{13}C NMR, $CDCl_3$, 75 MHz**)

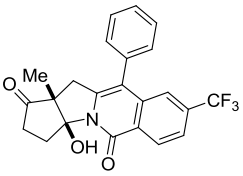
3a-Hydroxy-11a-methyl-10-phenyl-8-(trifluoromethyl)-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3y):



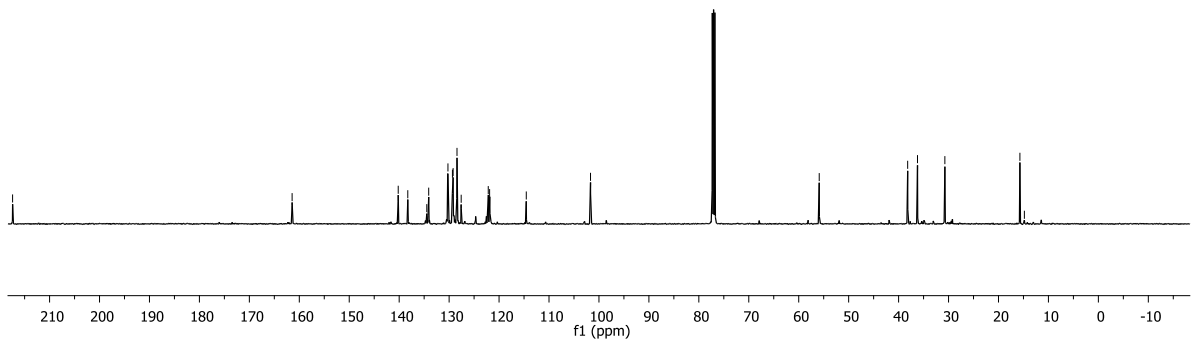
(**^{1}H NMR, $CDCl_3$, 500 MHz**)



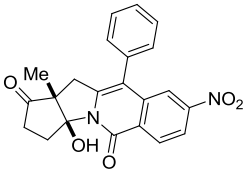




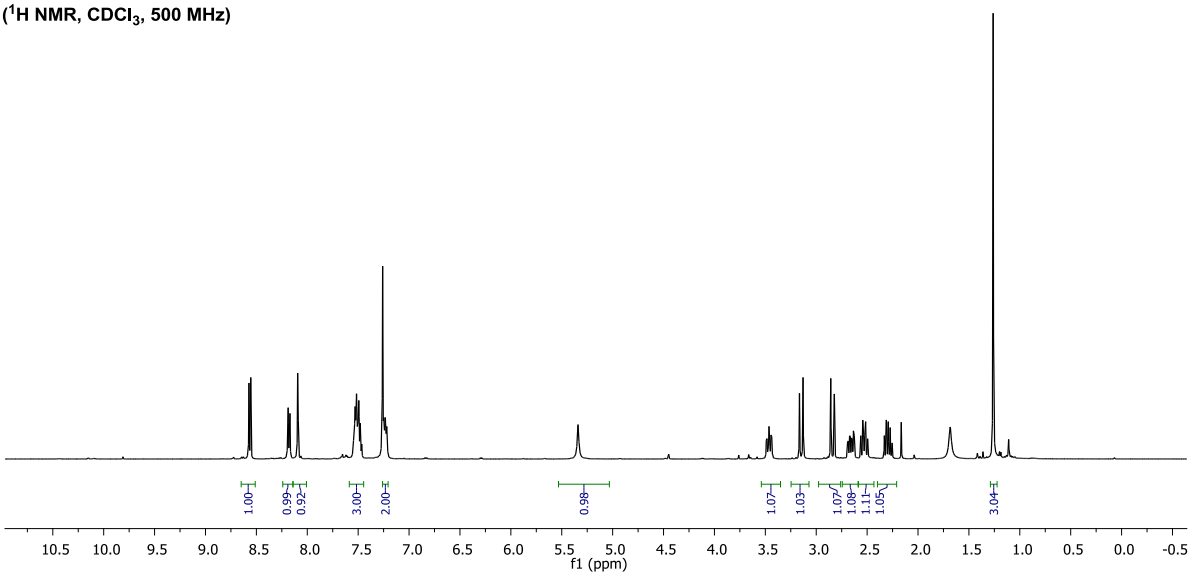
(**^{13}C NMR, $CDCl_3$, 125 MHz**)

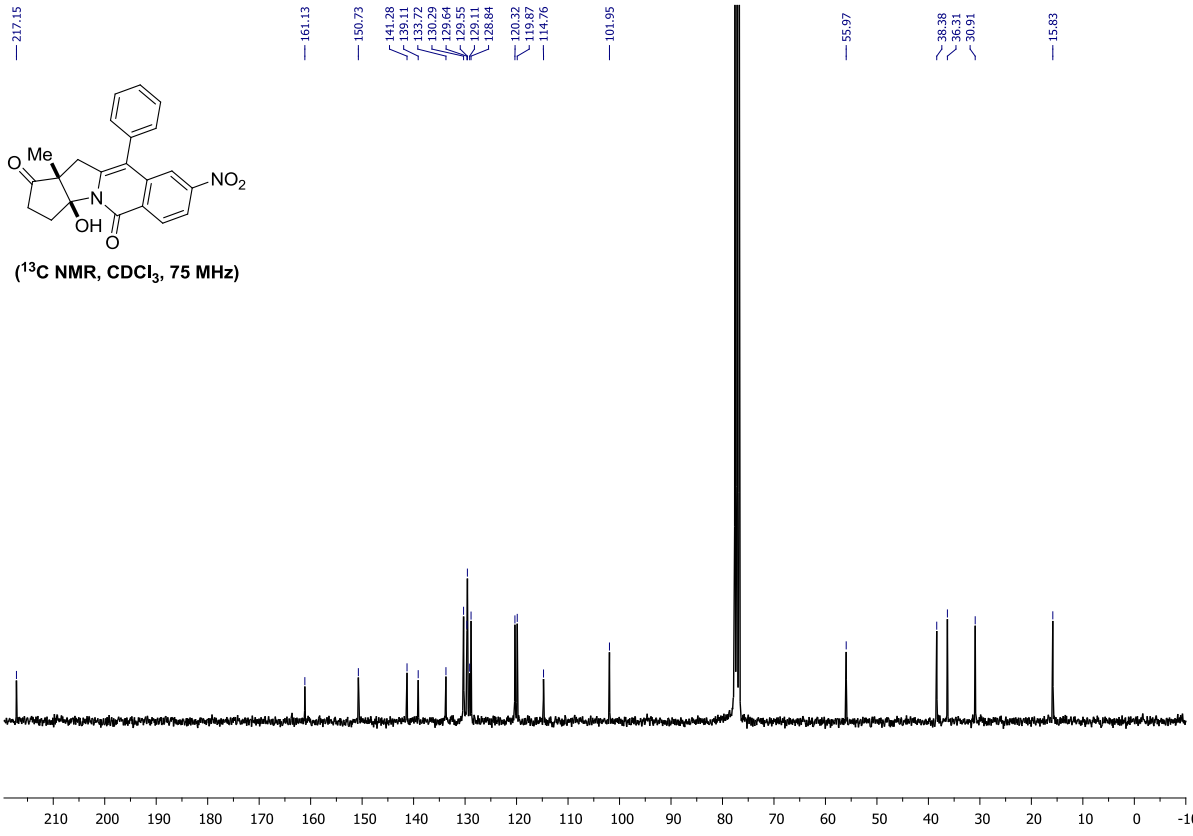


3a-Hydroxy-11a-methyl-8-nitro-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3z):



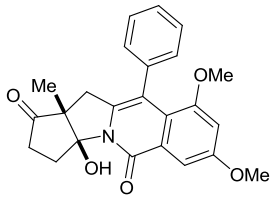
(^{1}H NMR, $CDCl_3$, 500 MHz)



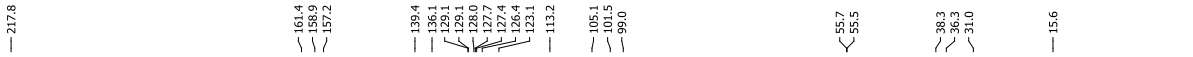


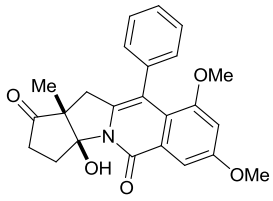
(^{13}C NMR, $CDCl_3$, 75 MHz)

3a-Hydroxy-7,9-dimethoxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3aa) :

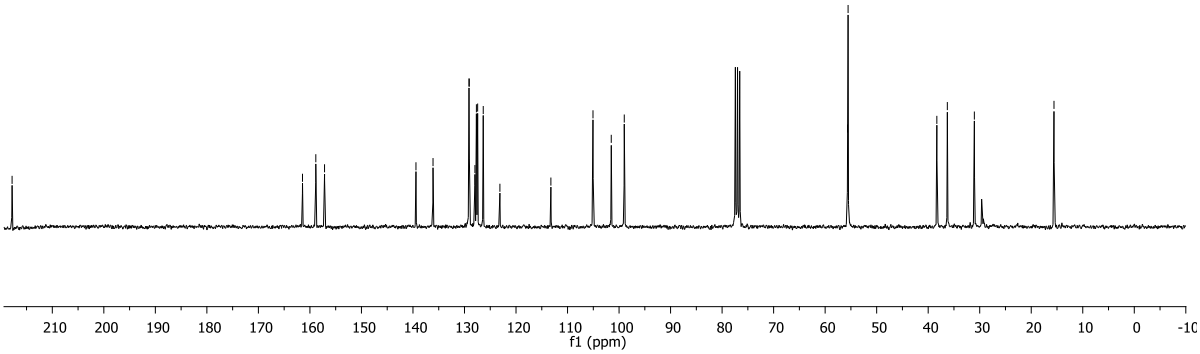


(¹H NMR, $CDCl_3$, 500 MHz)

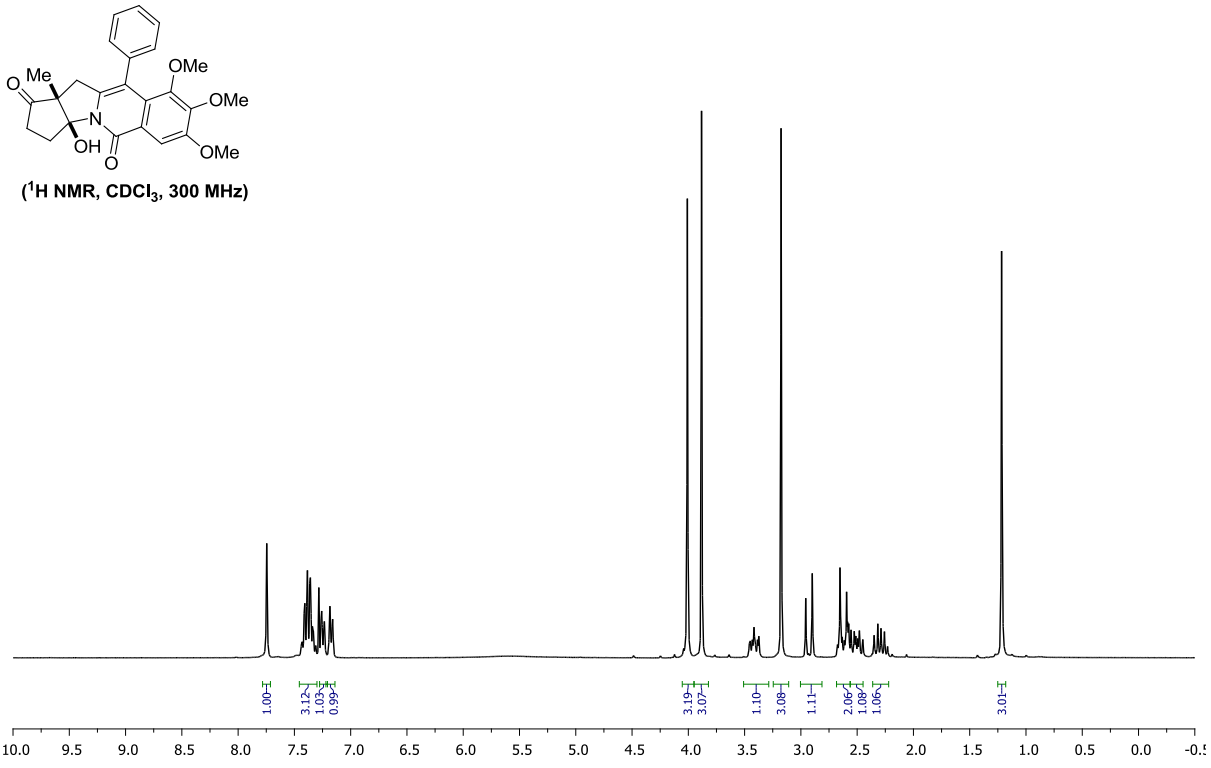


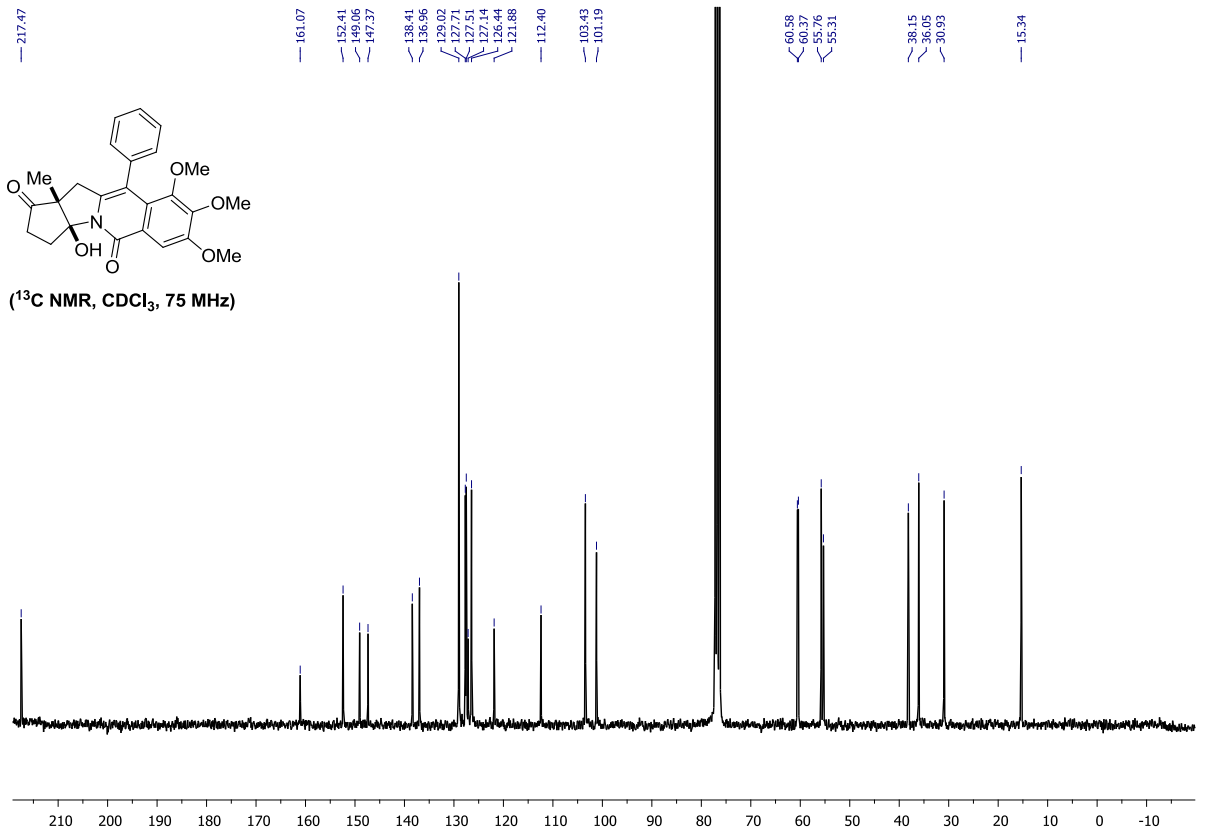


(¹³C NMR, $CDCl_3$, 75 MHz)

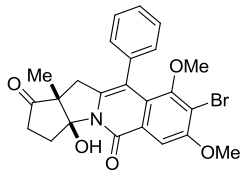


3a-Hydroxy-7,8,9-trimethoxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3ab):

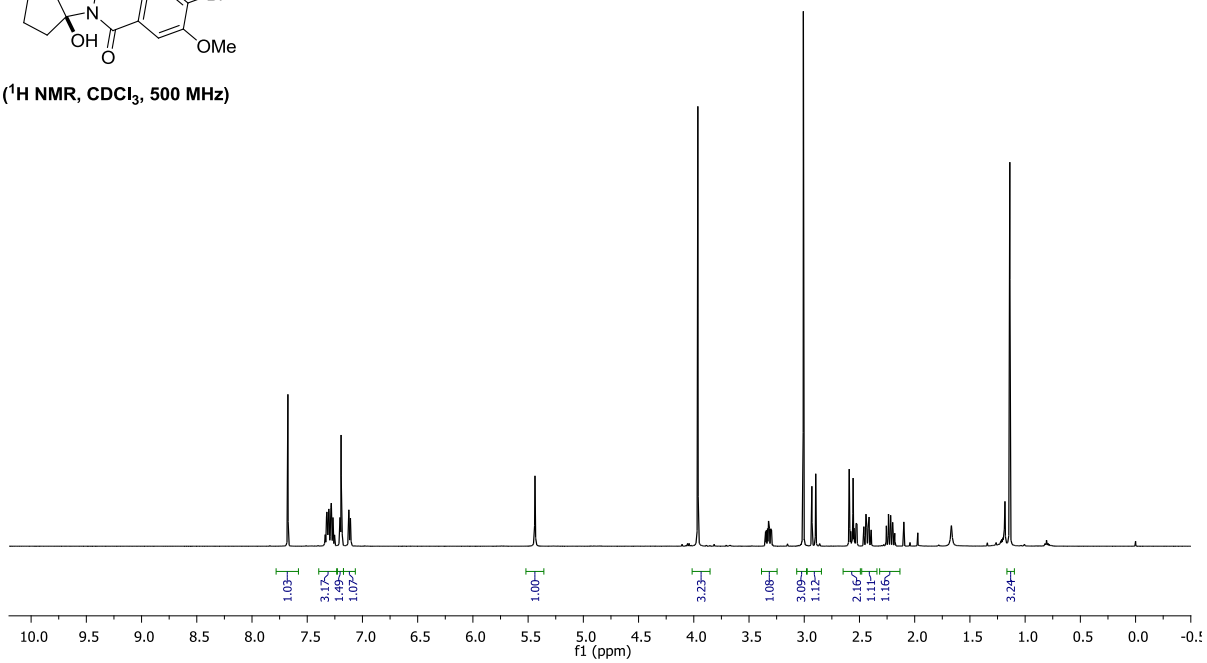


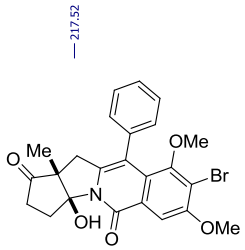


8-Bromo-3a-hydroxy-7,9-dimethoxy-11a-methyl-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3ac):



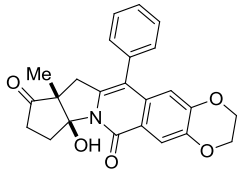
(**^{1}H NMR, $CDCl_3$, 500 MHz**)



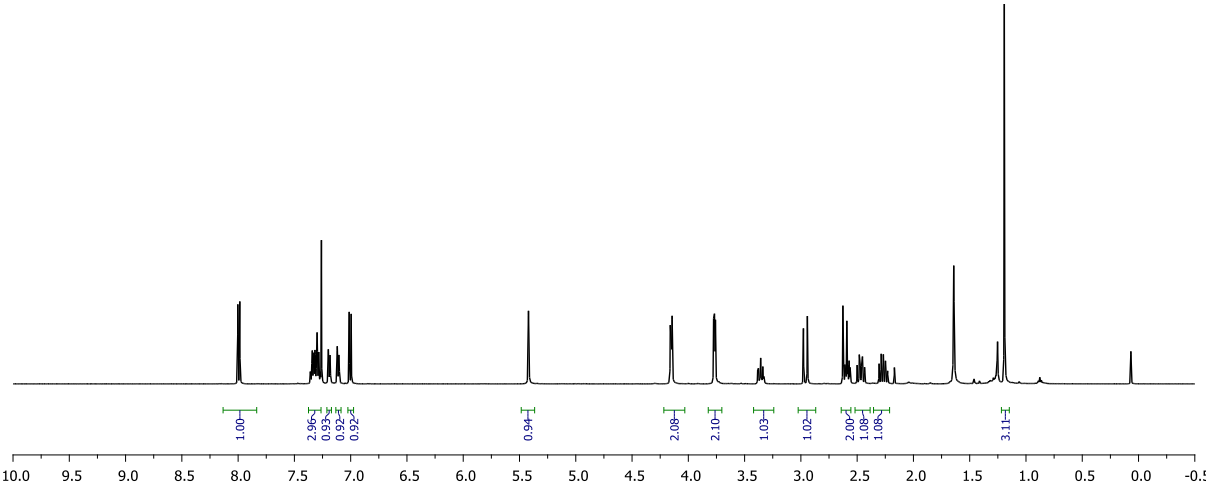


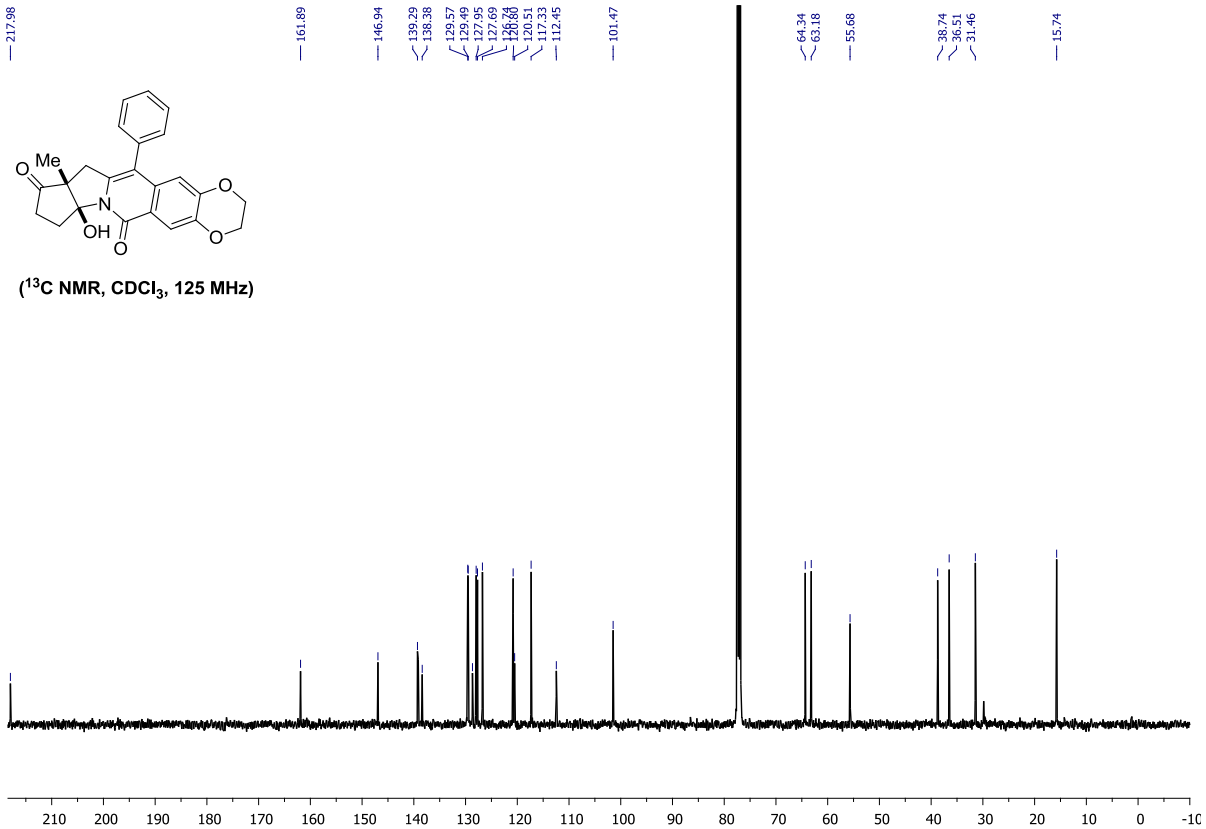
(**^{13}C NMR, $CDCl_3$, 125 MHz**)

7a-Hydroxy-10a-methyl-12-phenyl-8,9,10a,11-tetrahydro-2*H*-cyclopenta[4,5]pyrrolo[1,2-*b*][1,4]dioxino[2,3-*g*]isoquinoline-6,10(3*H*,7a*H*)-dione (3ad):



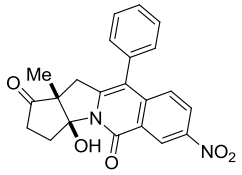
(^{1}H NMR, $CDCl_3$, 500 MHz)



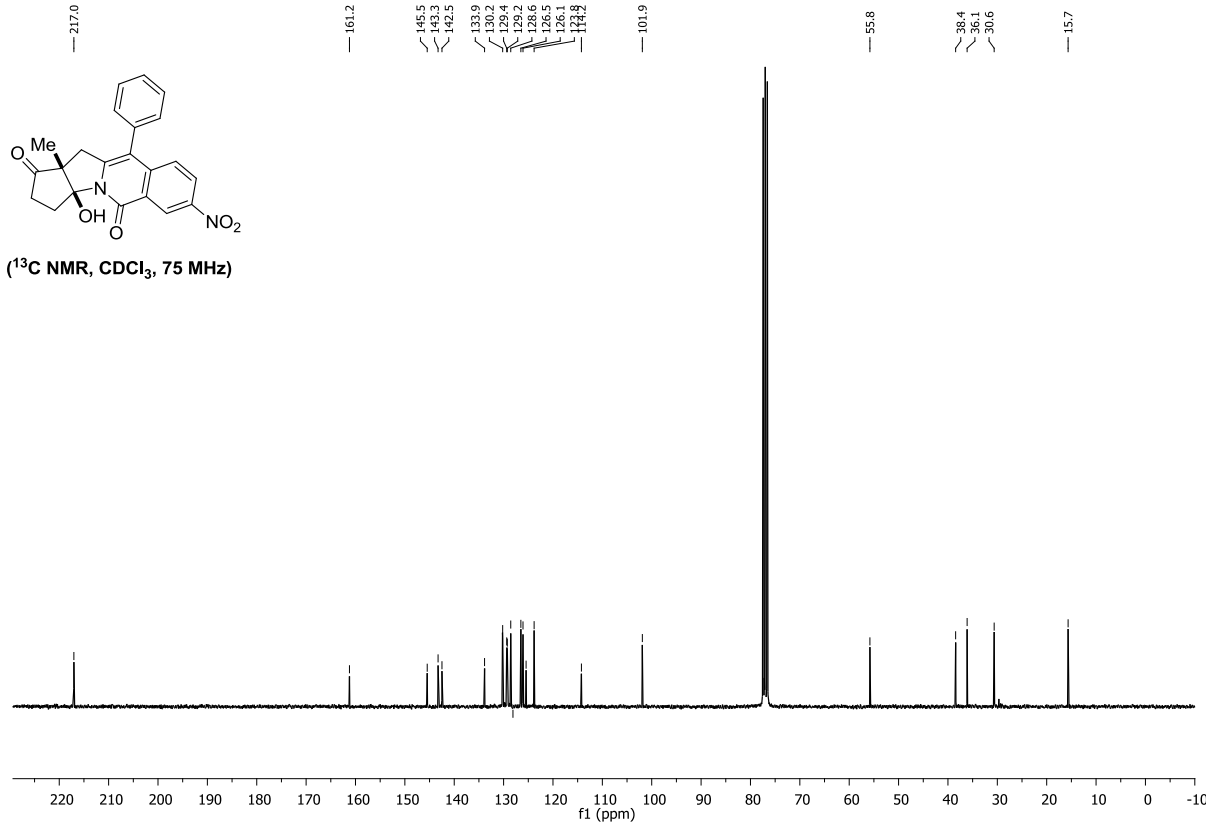


(^{13}C NMR, $CDCl_3$, 125 MHz)

3a-Hydroxy-11a-methyl-7-nitro-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3ae) :

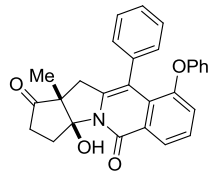


(**^{1}H NMR, $CDCl_3$, 500 MHz**)

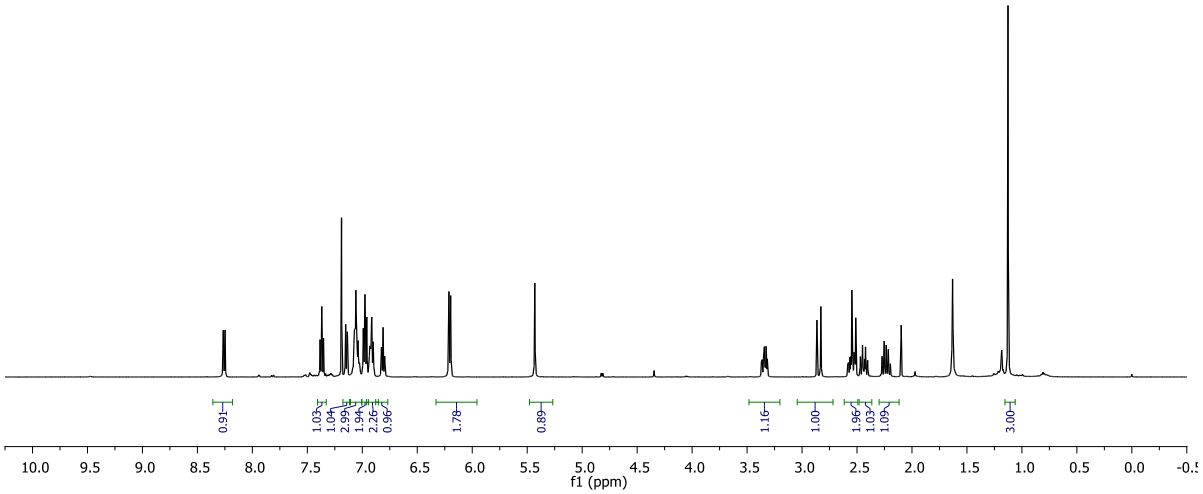


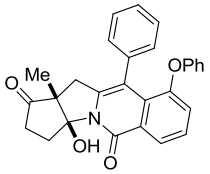
(**^{13}C NMR, $CDCl_3$, 75 MHz**)

3a-Hydroxy-11a-methyl-9-phenoxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3af) :

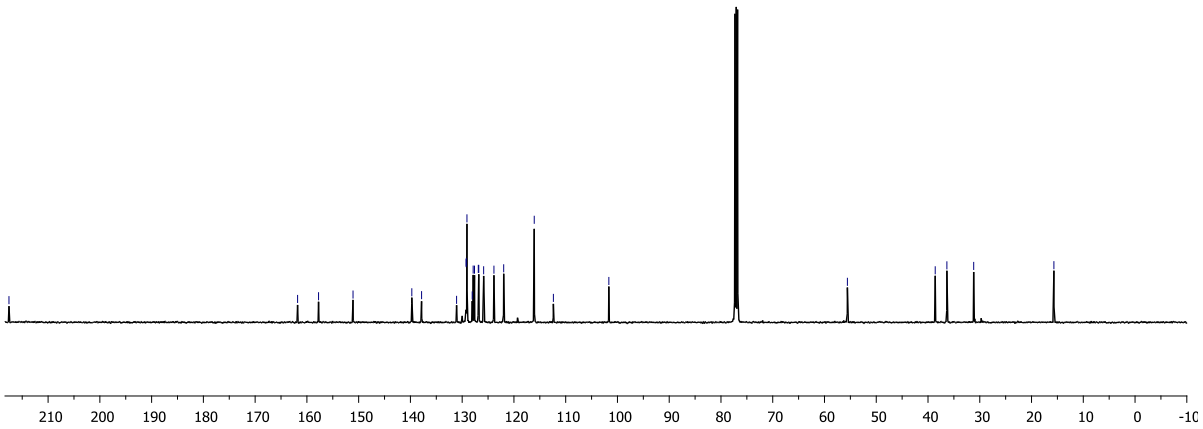


(^{1}H NMR, $CDCl_3$, 500 MHz)

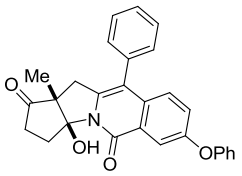




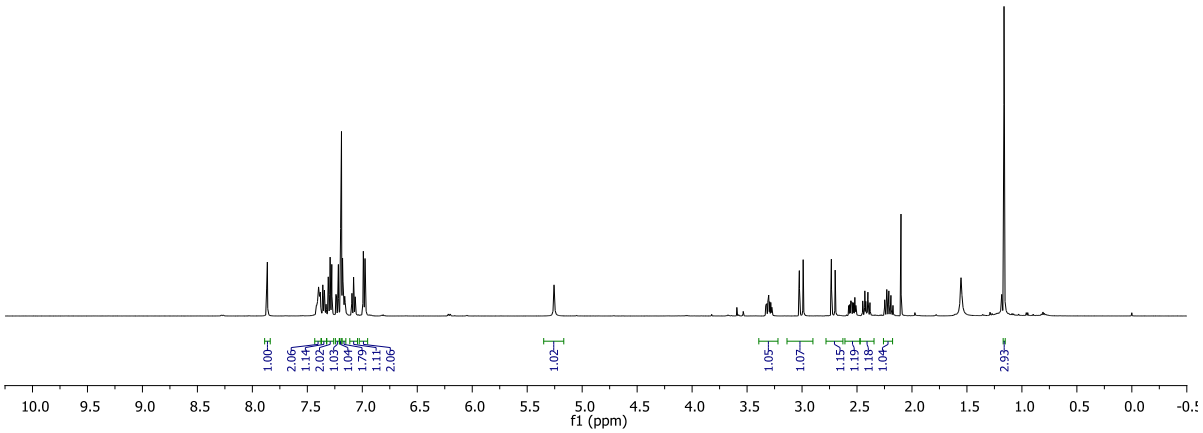
(^{13}C NMR, $CDCl_3$, 125 MHz)

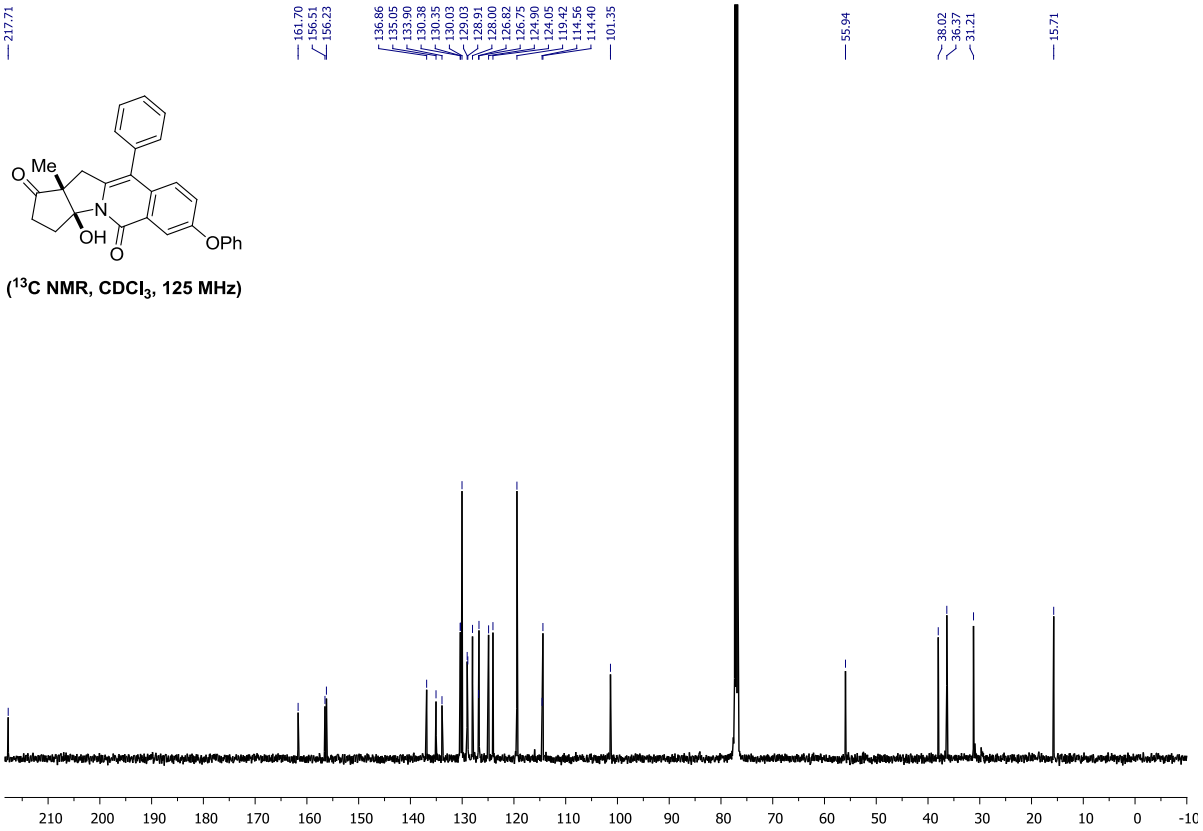


3a-Hydroxy-11a-methyl-7-phenoxy-10-phenyl-3,3a,11,11a-tetrahydro-1*H*-cyclopenta[4,5]pyrrolo[1,2-*b*]isoquinoline-1,5(2*H*)-dione (3af[1]):



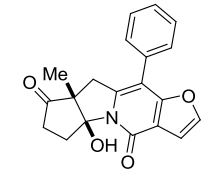
(**^{1}H NMR, $CDCl_3$, 500 MHz**)



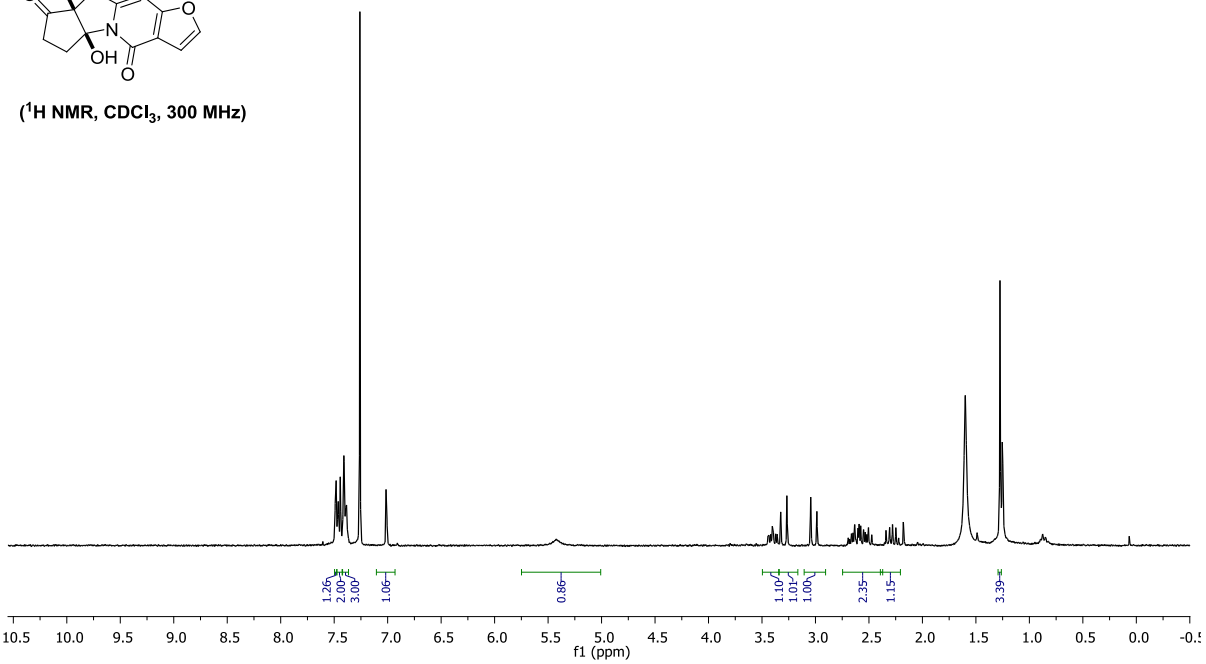


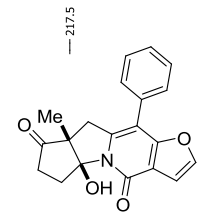
(**^{13}C NMR, $CDCl_3$, 125 MHz**)

5a-Hydroxy-8a-methyl-10-phenyl-6,7,8a,9-tetrahydro-4*H*-cyclopenta[*b*]furo[3,2-*f*]indolizine-4,8(5a*H*)-dione (3ag) :



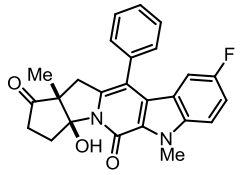
(^{1}H NMR, $CDCl_3$, 300 MHz)



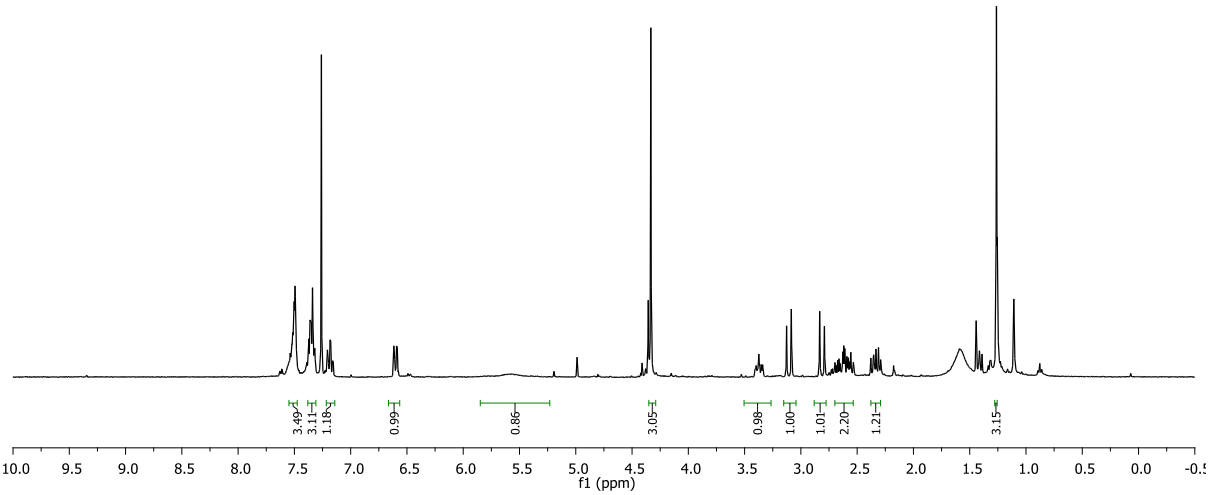


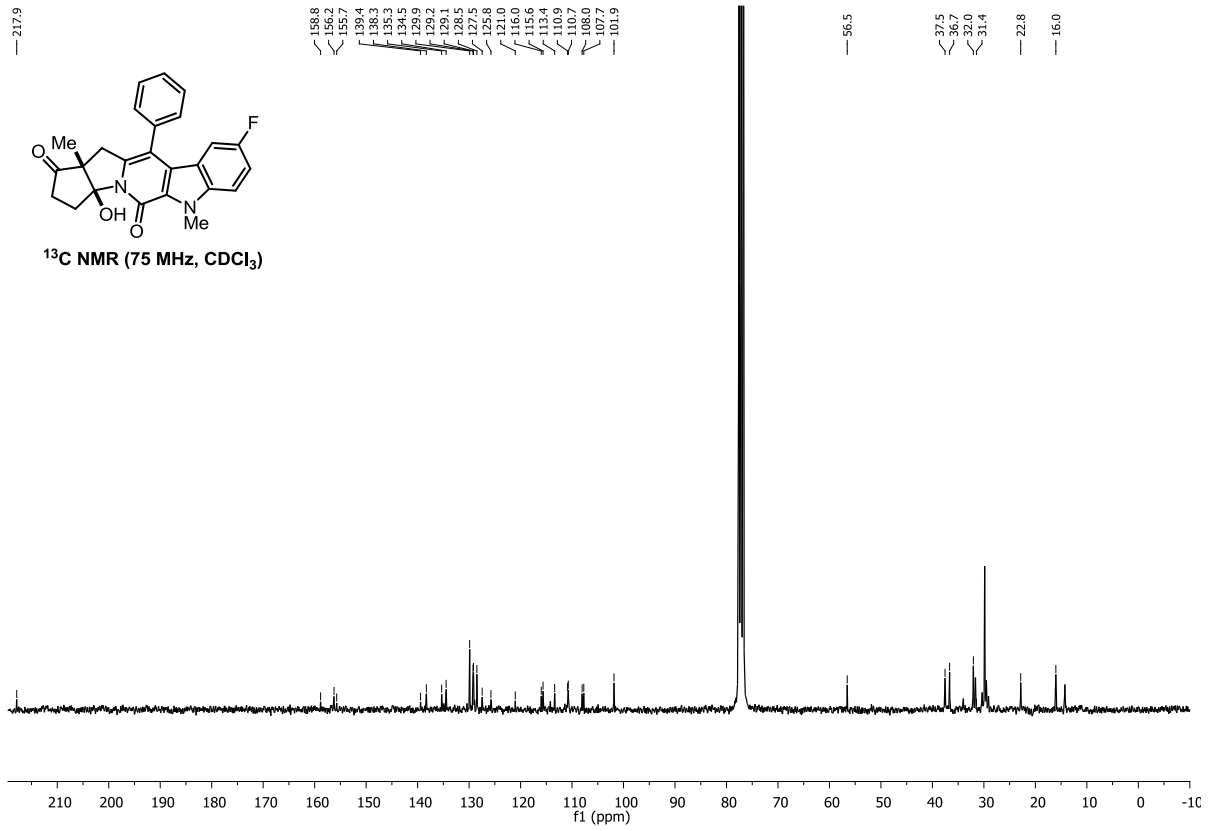
(^{13}C NMR, $CDCl_3$, 125 MHz)

9-Fluoro-3a-hydroxy-6,12a-dimethyl-11-phenyl-3,3a,12,12a-tetrahydrocyclopenta[2,3]indolizino[6,7-b]indole-1,5(2H,6H)-dione (3ah):



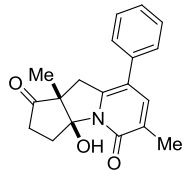
^{1}H NMR (400 MHz, $CDCl_3$)



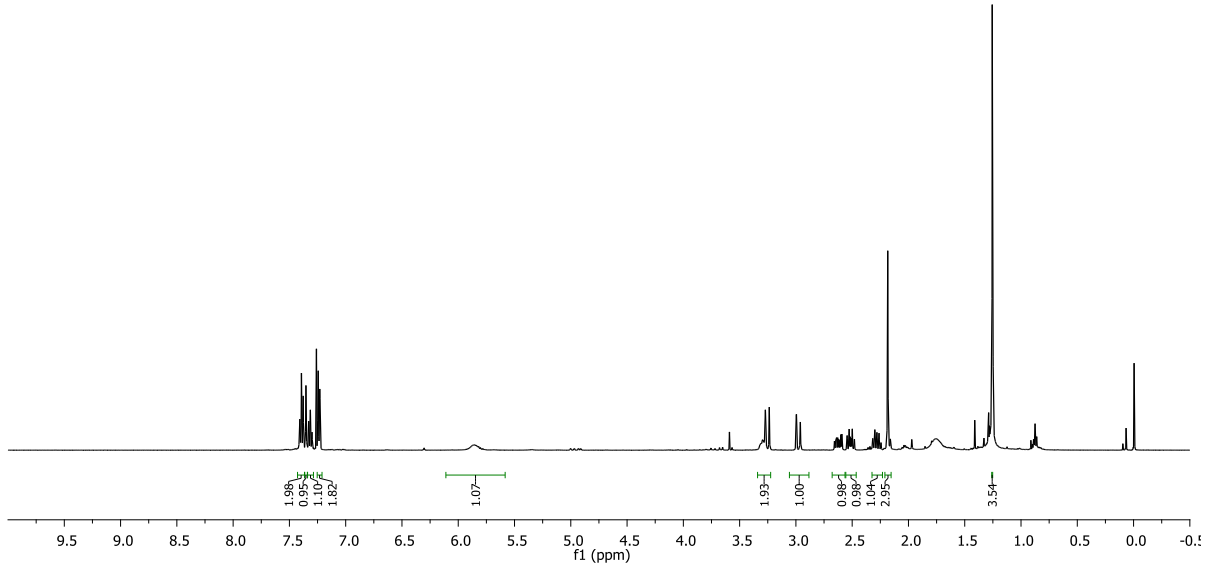


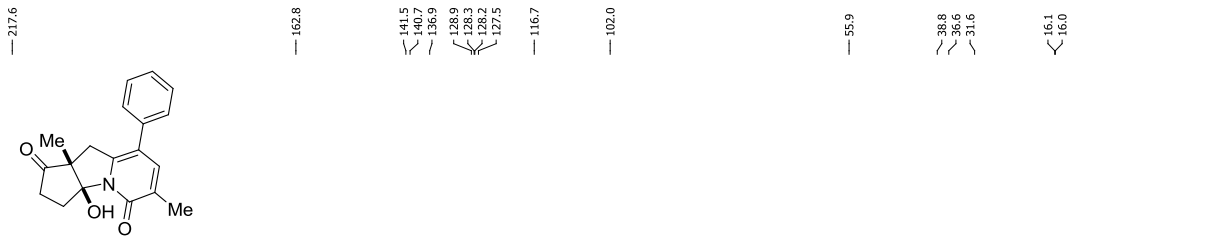
^{13}C NMR (75 MHz, $CDCl_3$)

3a-Hydroxy-6,9a-dimethyl-8-phenyl-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3ai):

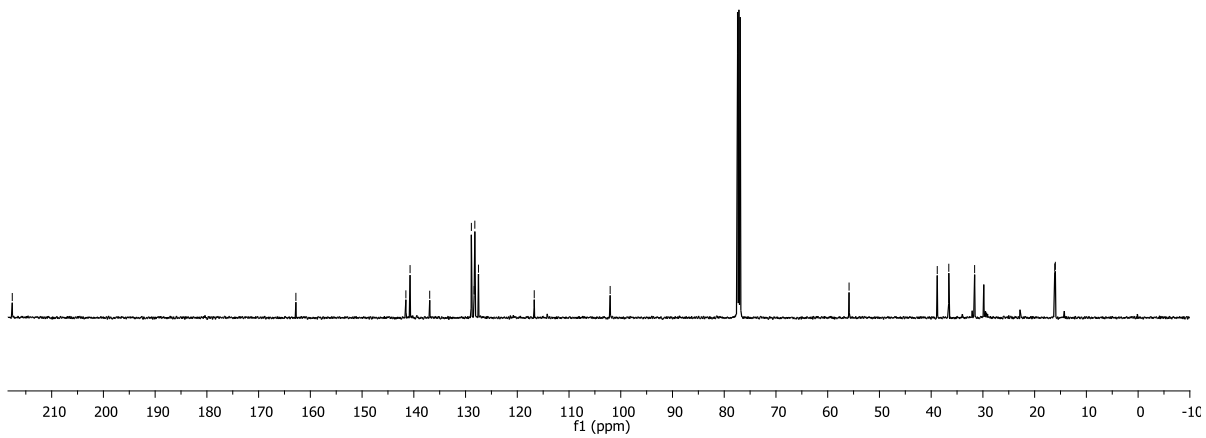


(**^{1}H NMR, $CDCl_3$, 500 MHz**)

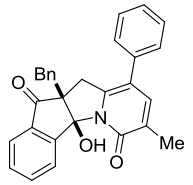




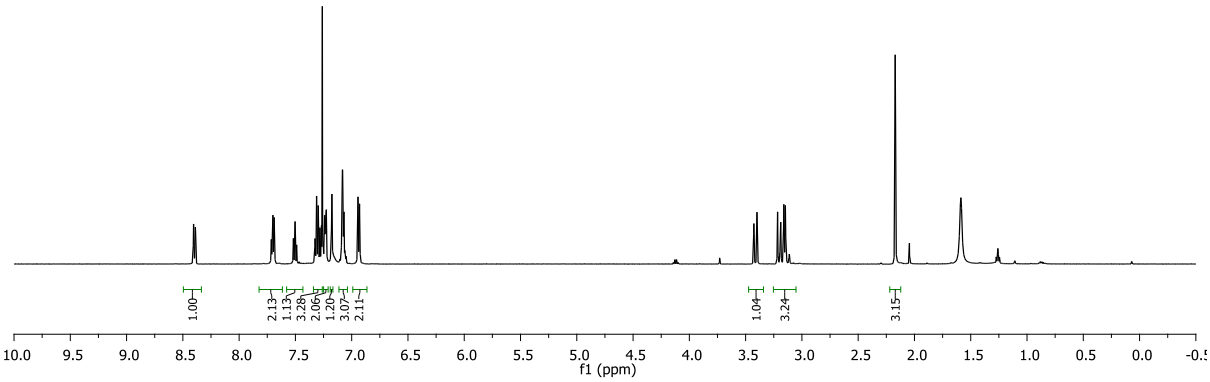
(**^{13}C NMR, $CDCl_3$, 125 MHz**)

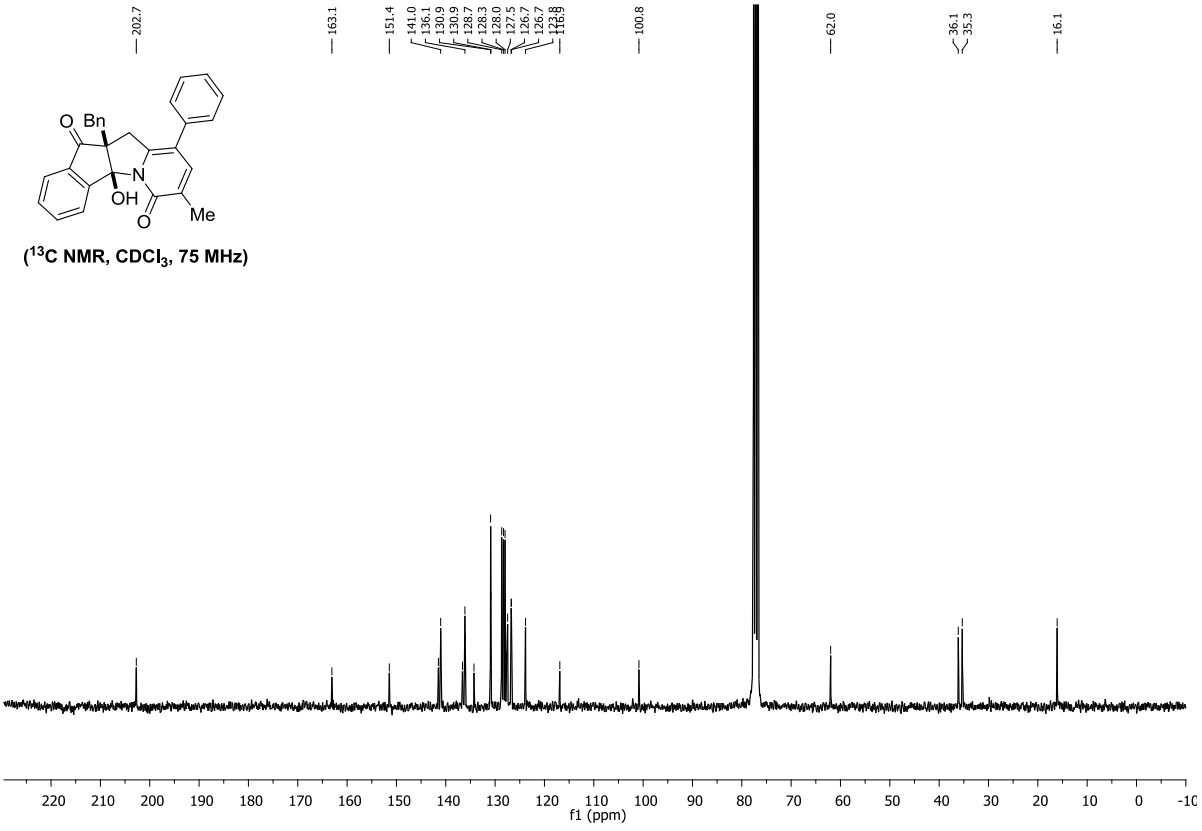


10a-Benzyl-4b-hydroxy-7-methyl-9-phenyl-10,10a-dihydro-4b*H*-indeno[2,1-*b*]indolizine-6,11-dione (3aj):



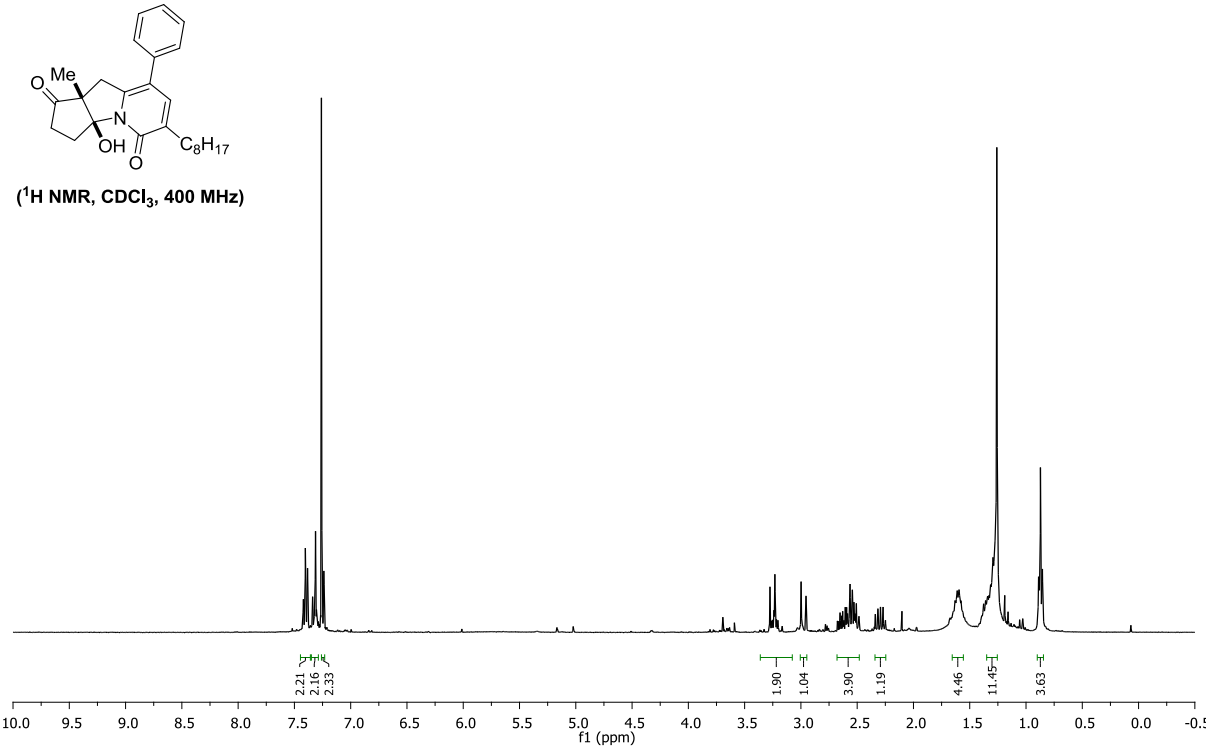
(**^{1}H NMR, $CDCl_3$, 500 MHz**)



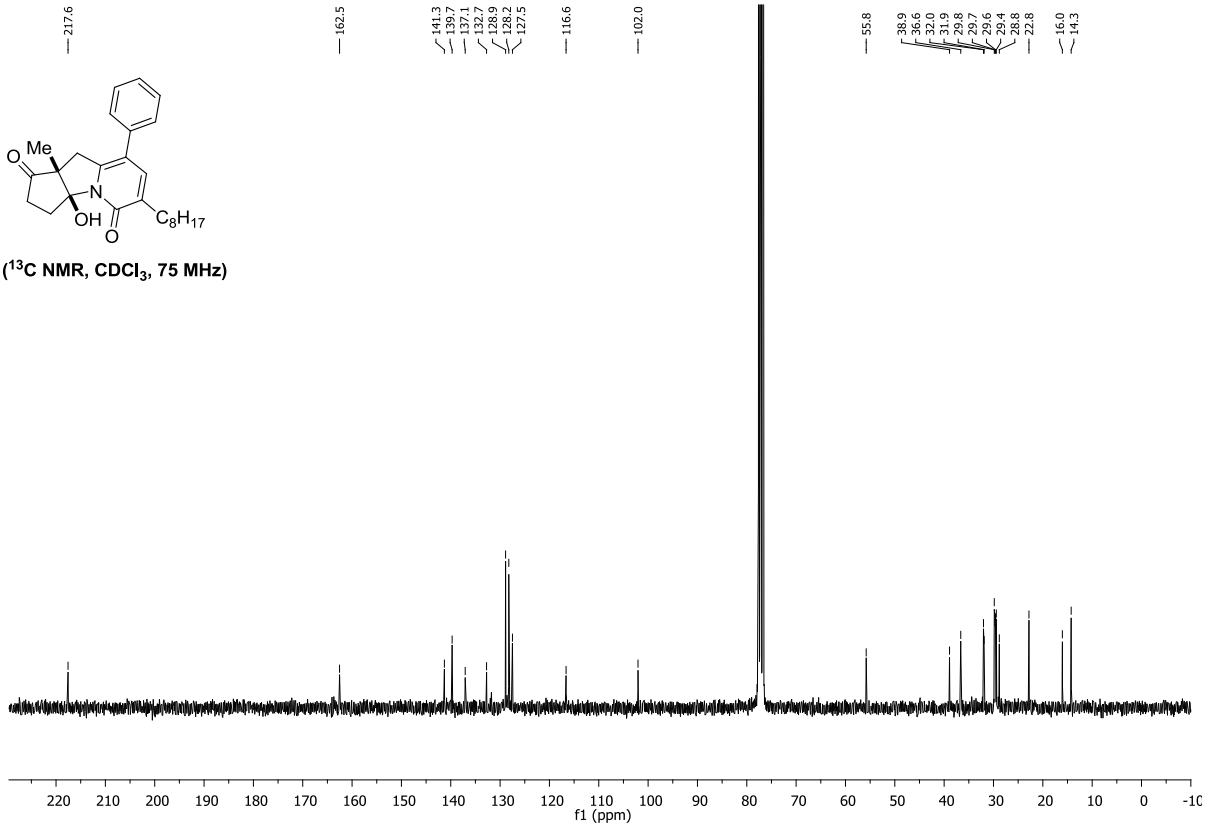


(**^{13}C NMR, $CDCl_3$, 75 MHz**)

3a-Hydroxy-9a-methyl-6-octyl-8-phenyl-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3ak):

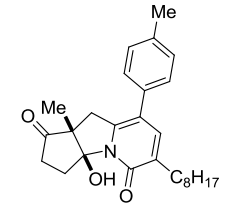


(^{1}H NMR, $CDCl_3$, 400 MHz)

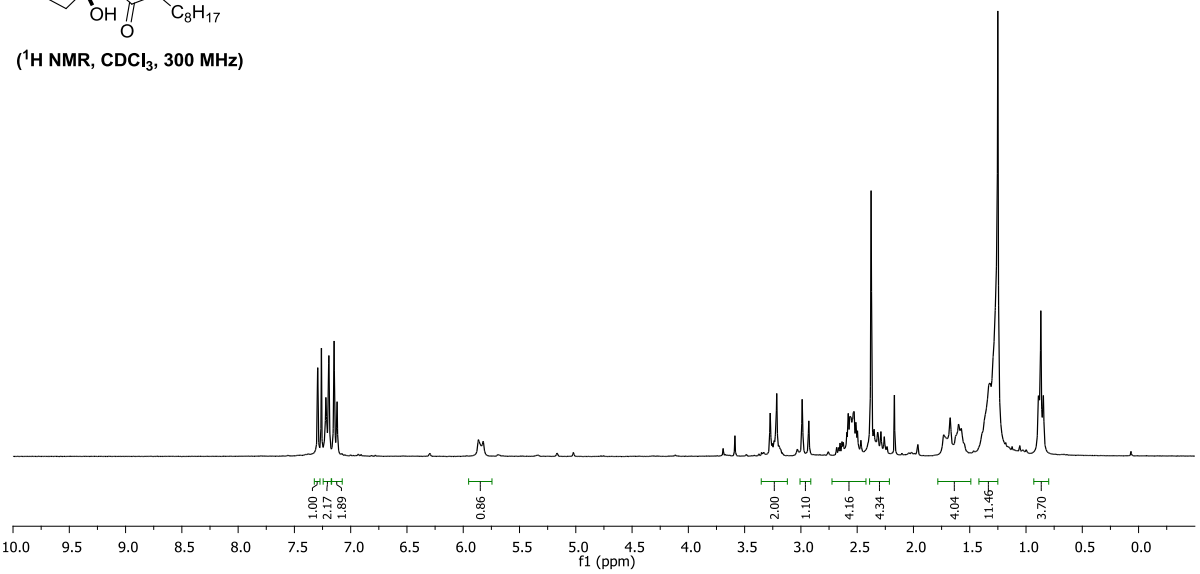


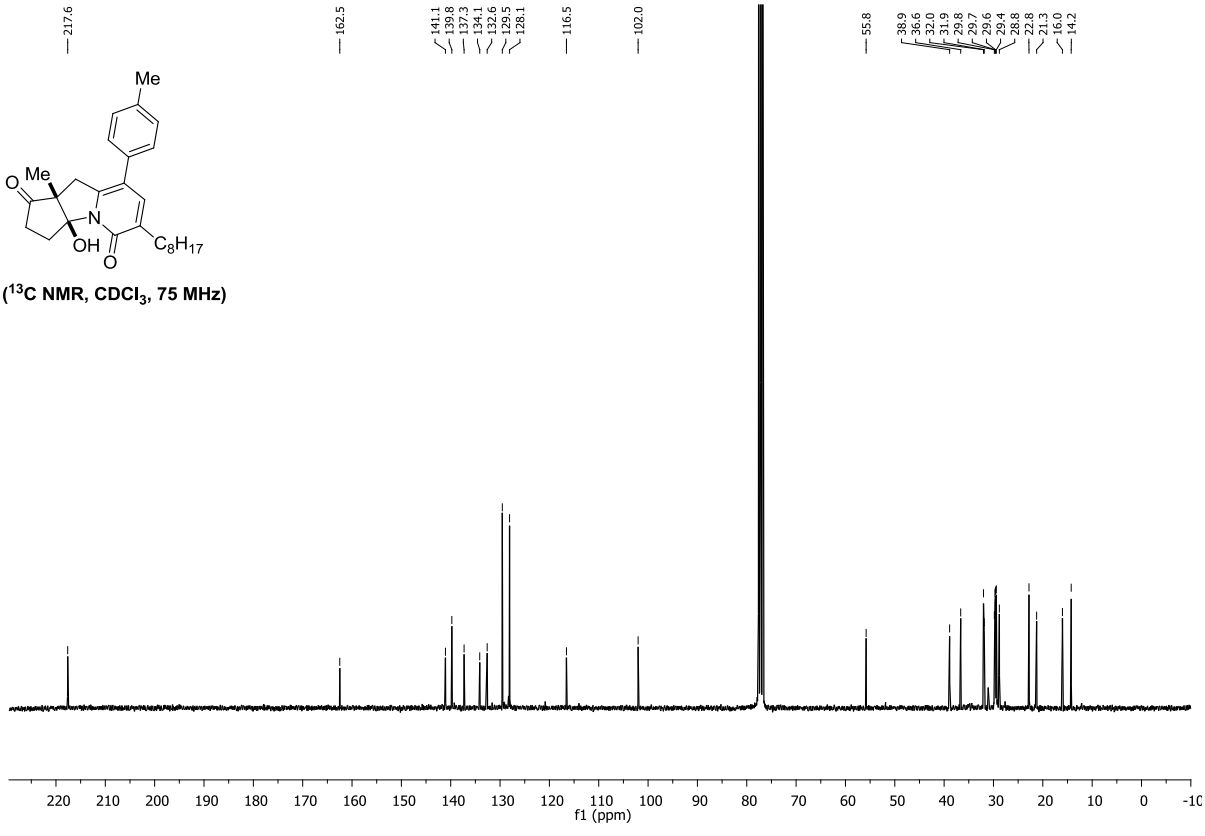
(^{13}C NMR, $CDCl_3$, 75 MHz)

3a-Hydroxy-9a-methyl-6-octyl-8-(*p*-tolyl)-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3al):



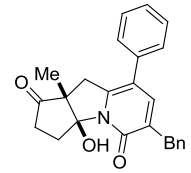
(^{1}H NMR, $CDCl_3$, 300 MHz)



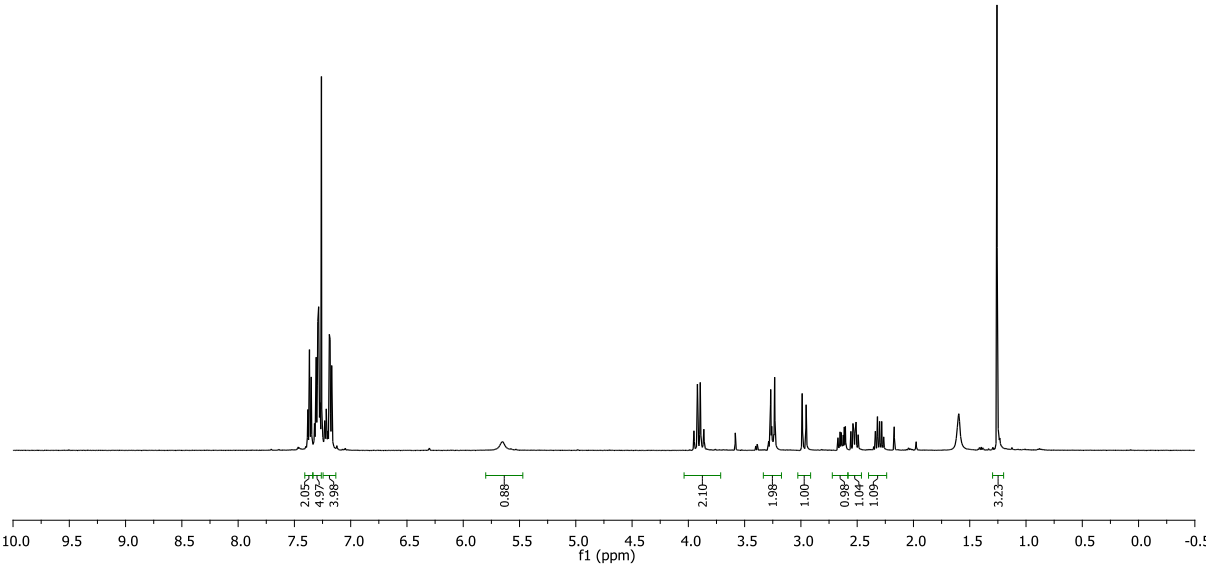


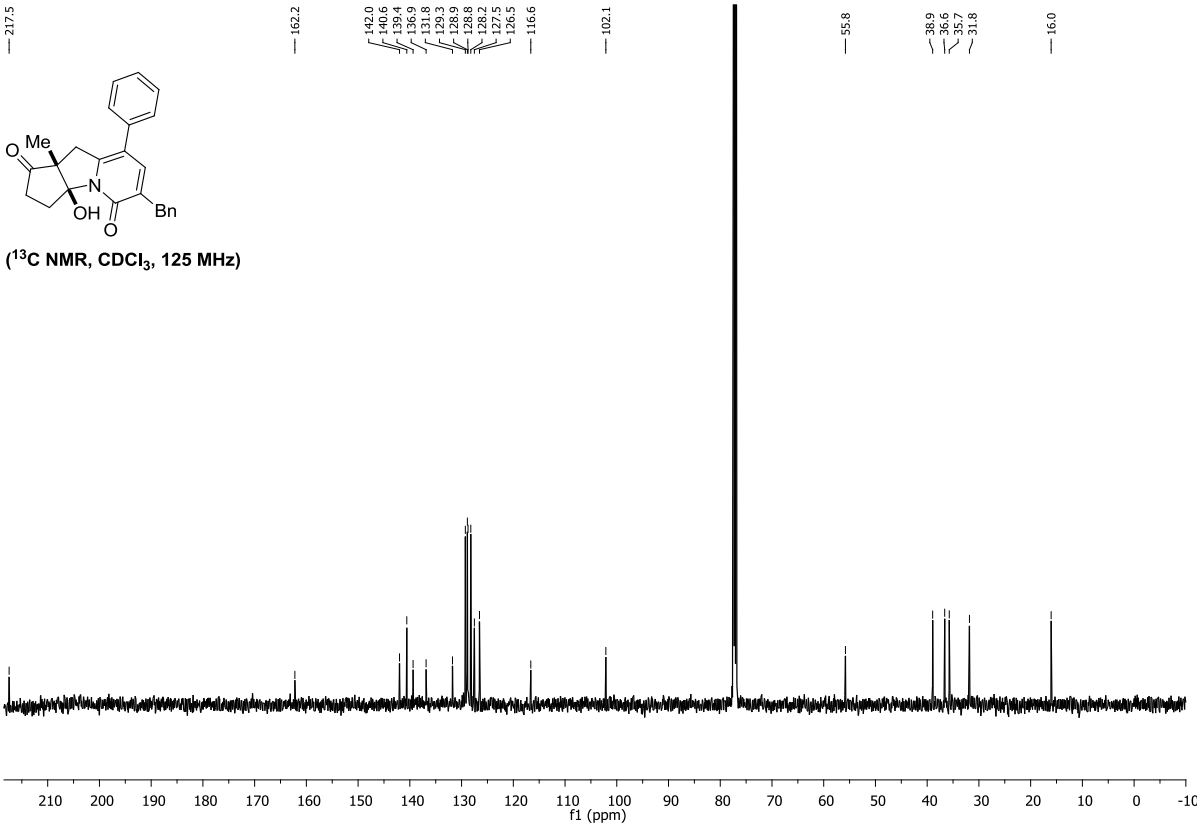
(^{13}C NMR, $CDCl_3$, 75 MHz)

6-Benzyl-3a-hydroxy-9a-methyl-8-phenyl-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3am):



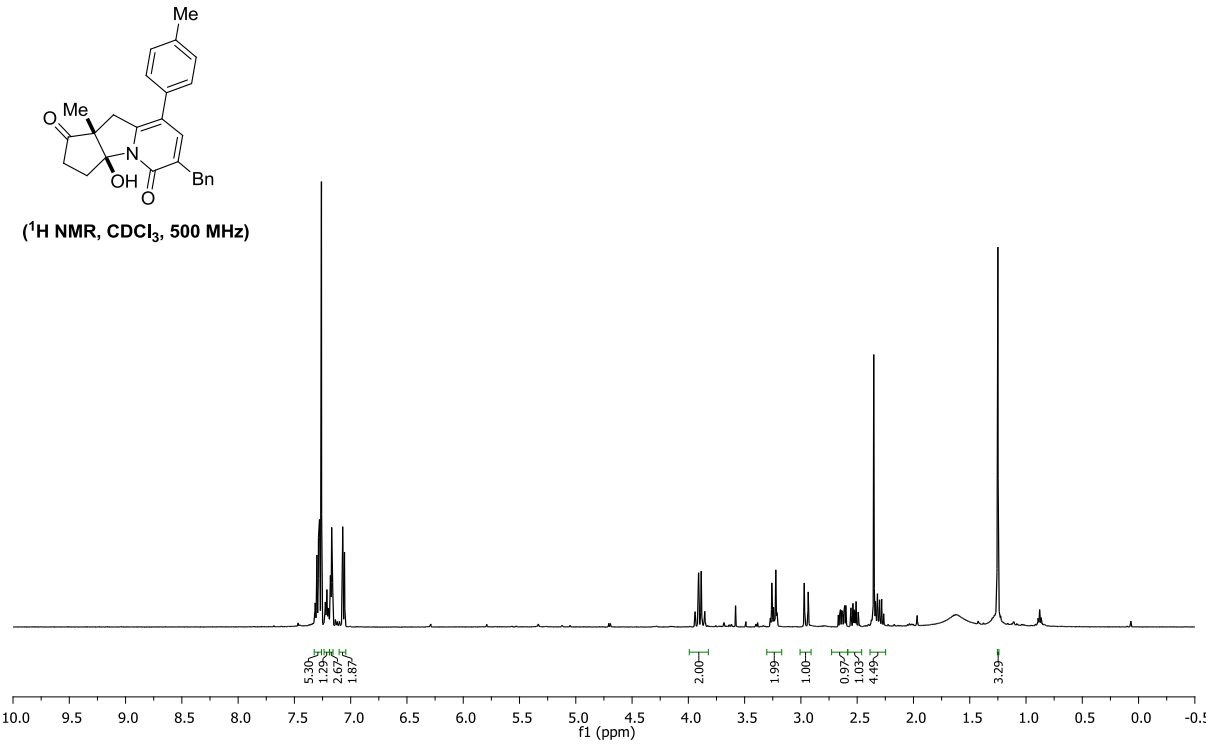
(^{1}H NMR, $CDCl_3$, 500 MHz)

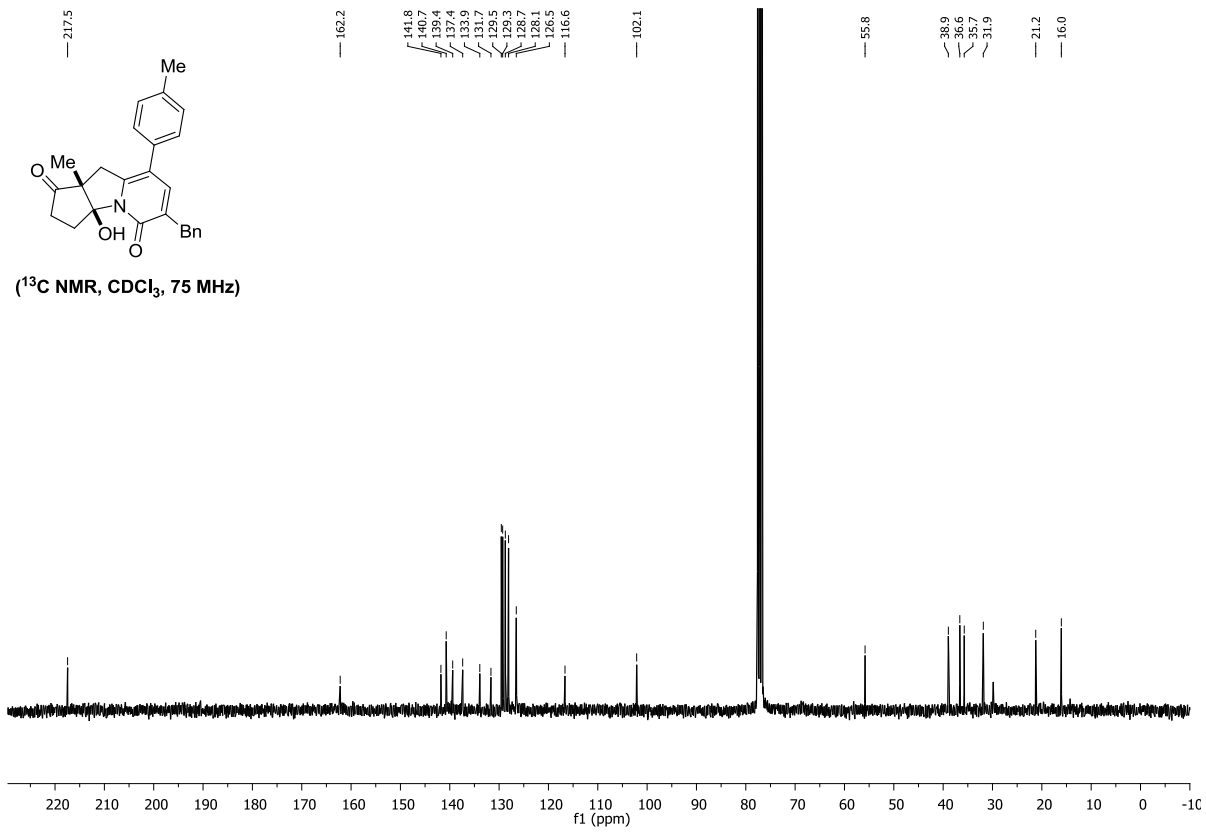




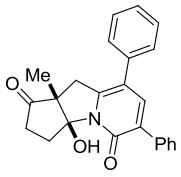
(^{13}C NMR, $CDCl_3$, 125 MHz)

6-Benzyl-3a-hydroxy-9a-methyl-8-(p-tolyl)-3,3a,9,9a-tetrahydro-1H-cyclopenta[b]indolizine-1,5(2H)-dione(3an):

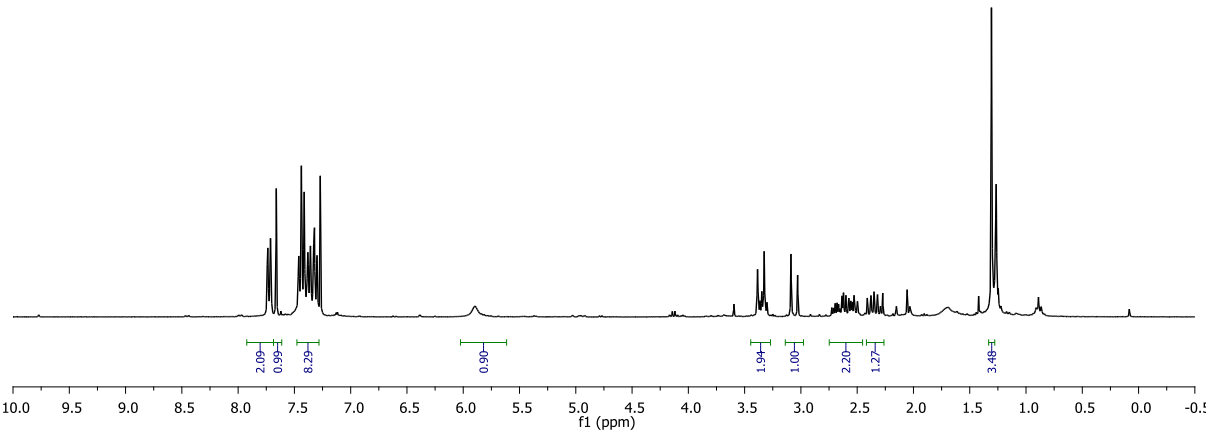


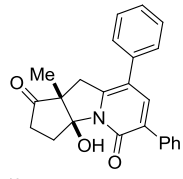


3a-Hydroxy-9a-methyl-6,8-diphenyl-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione(3ao):



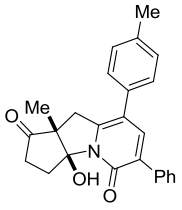
(^{1}H NMR, $CDCl_3$, 300 MHz)



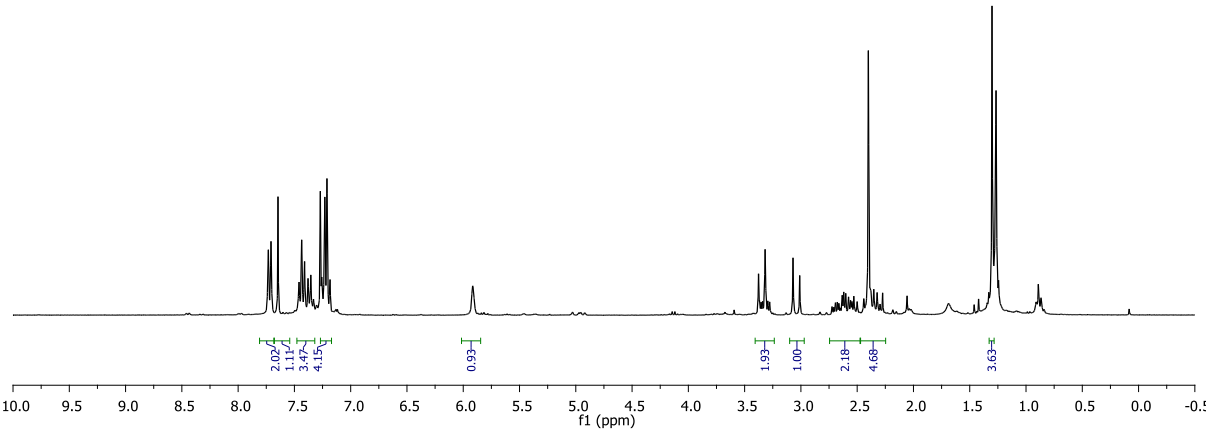


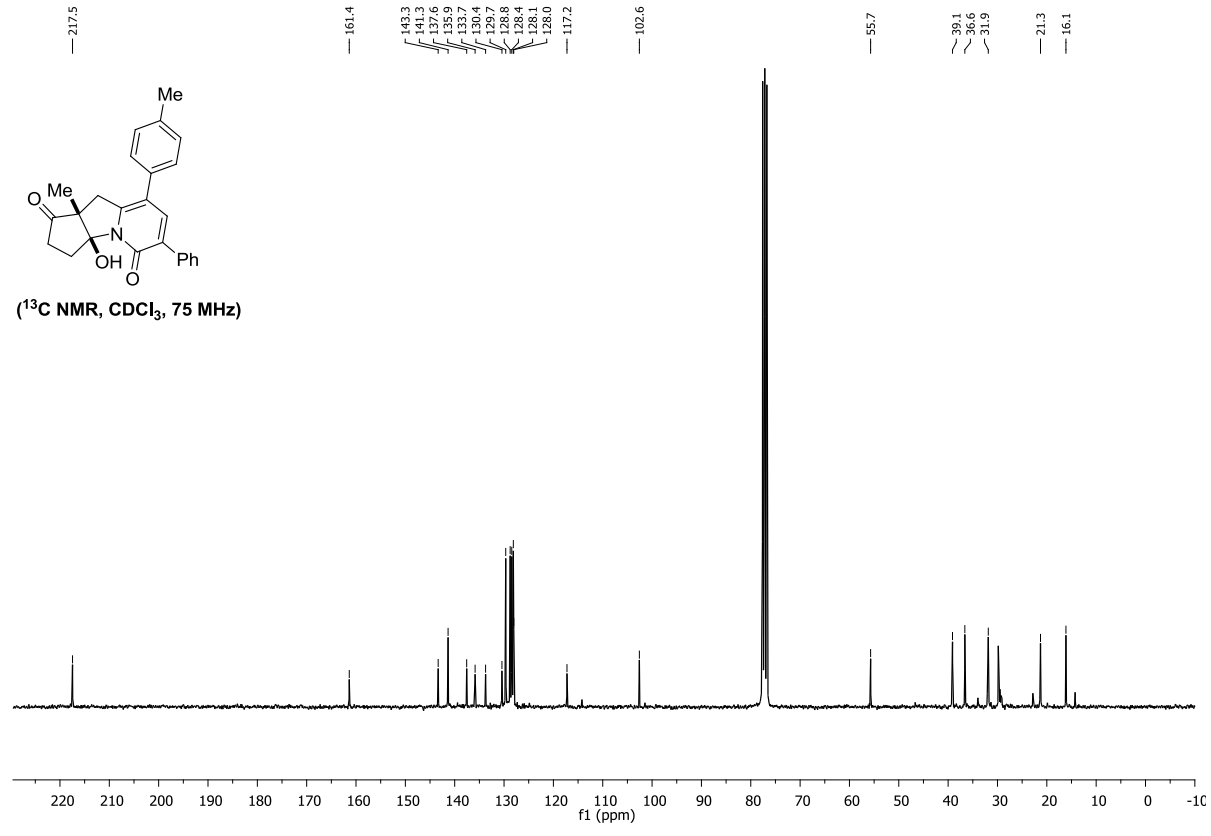
(^{13}C NMR, $CDCl_3$, 75 MHz)

3a-Hydroxy-9a-methyl-6-phenyl-8-(*p*-tolyl)-3,3a,9,9a-tetrahydro-1*H*-cyclopenta[*b*]indolizine-1,5(2*H*)-dione (3ap):



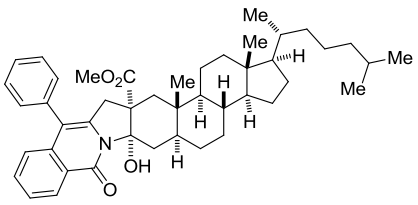
(^{1}H NMR, $CDCl_3$, 300 MHz)



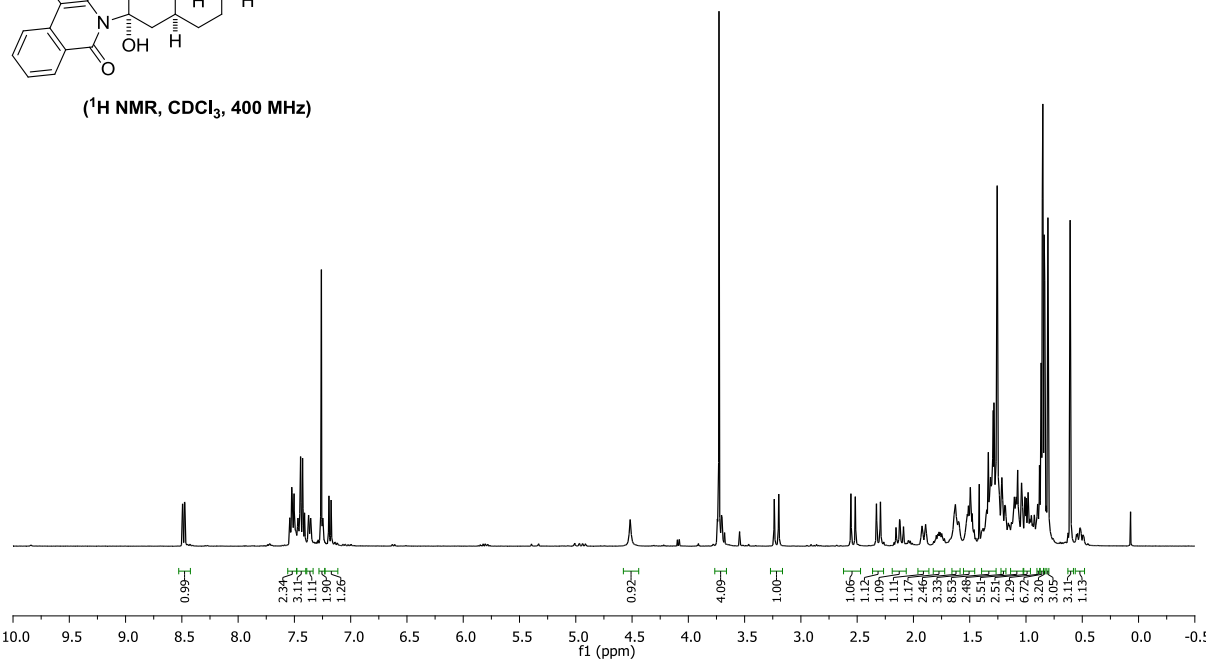


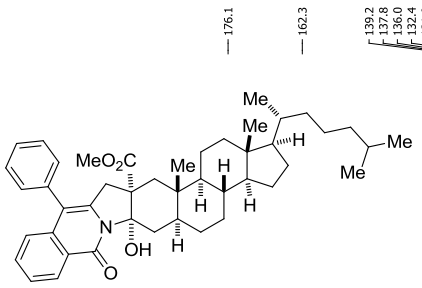
(^{13}C NMR, $CDCl_3$, 75 MHz)

Compound 5a data:



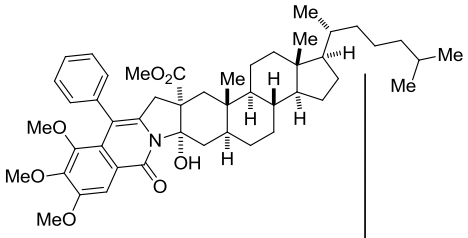
(¹H NMR, $CDCl_3$, 400 MHz)



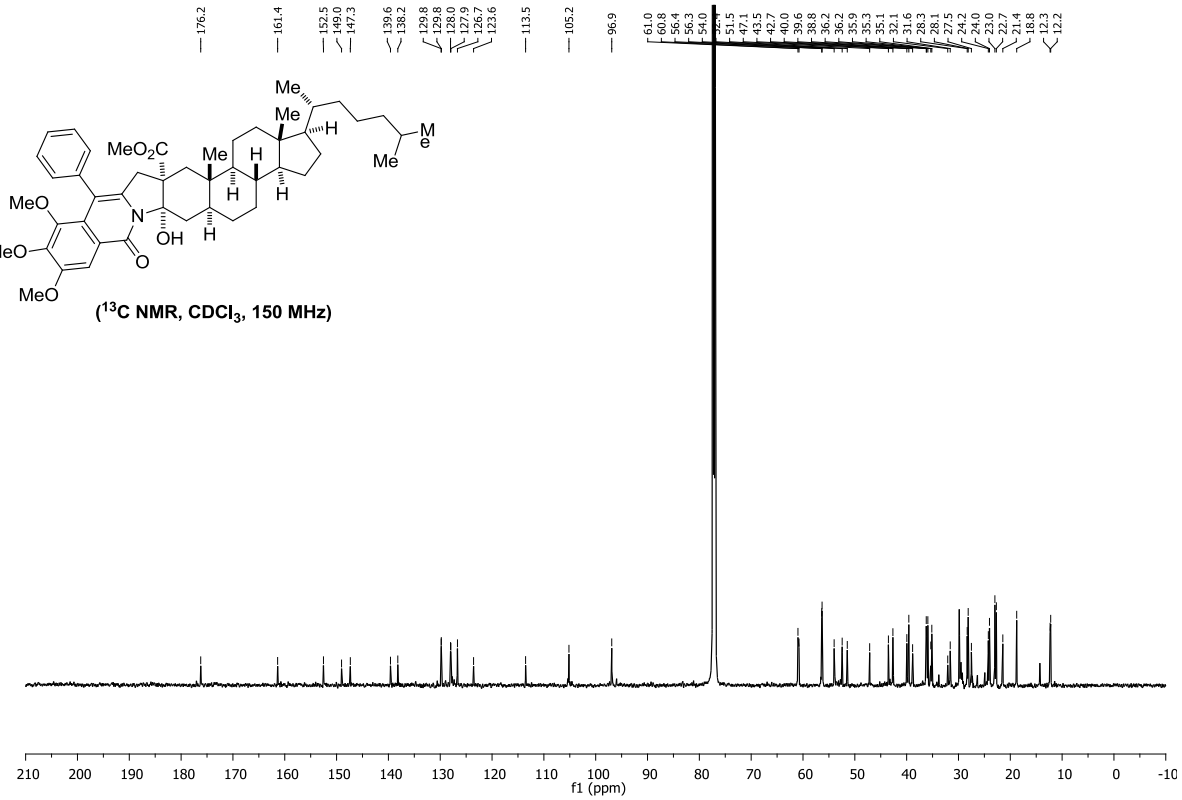


(¹³C NMR, $CDCl_3$, 125 MHz)

Compound 5b data:

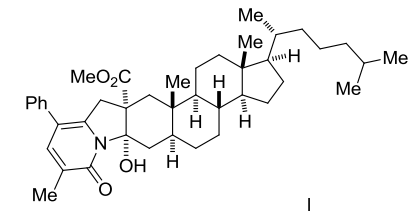


(^{1}H NMR, $CDCl_3$, 500 MHz)

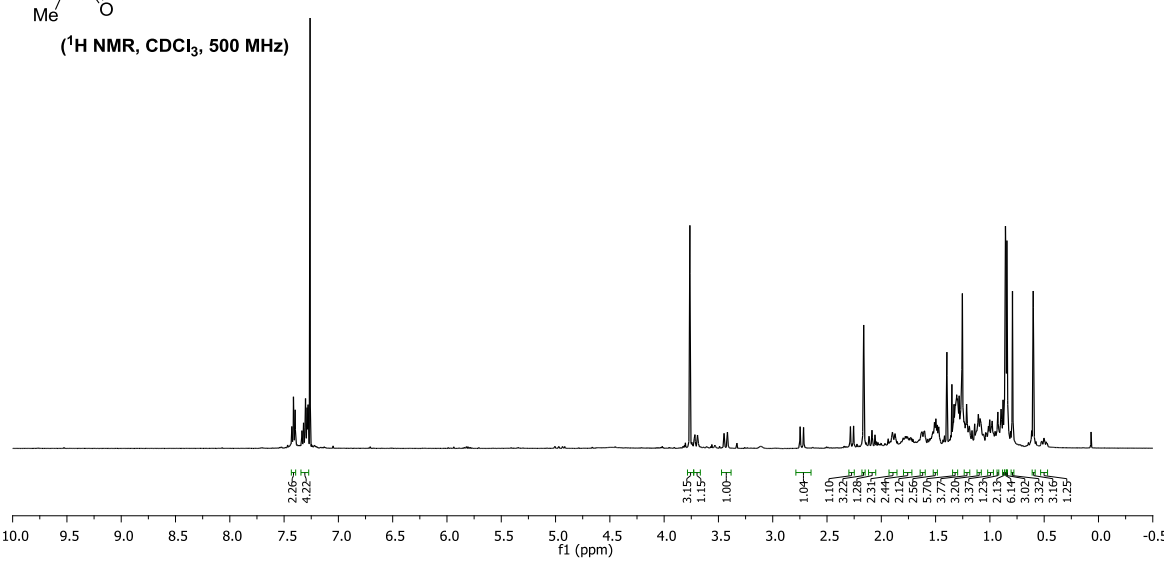


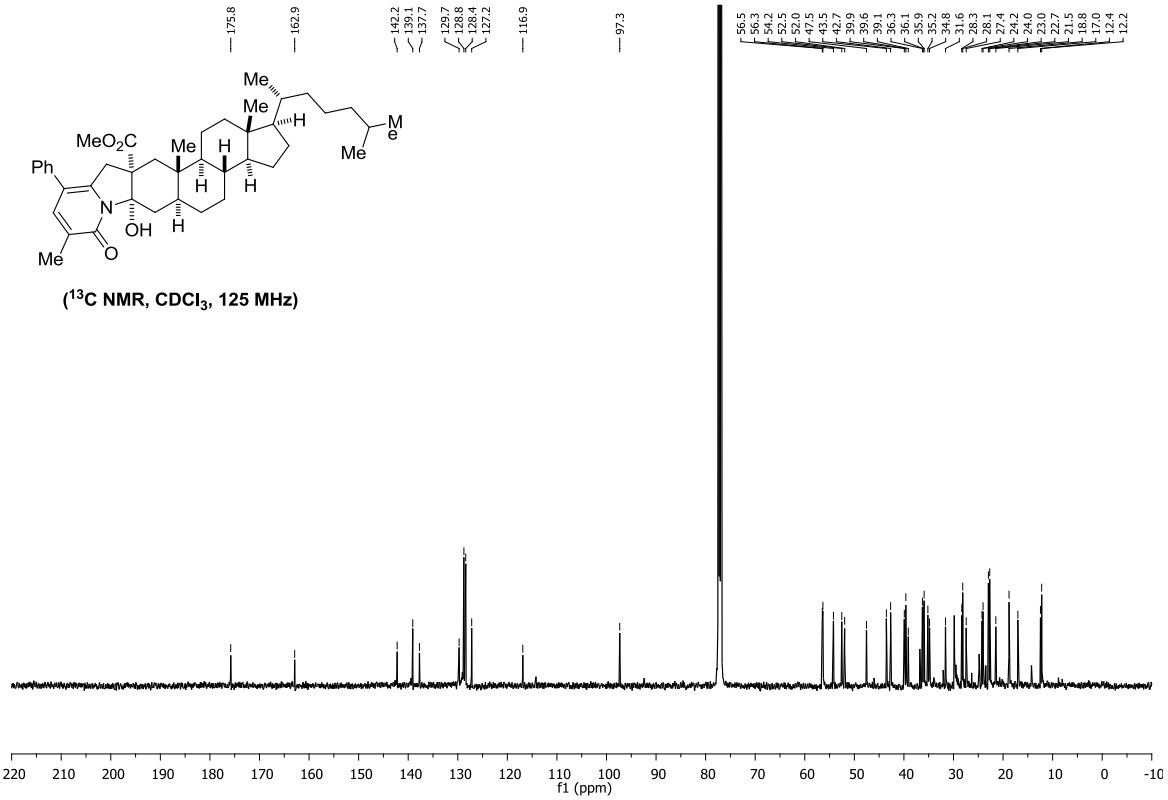
(^{13}C NMR, $CDCl_3$, 150 MHz)

Compound 5c data:



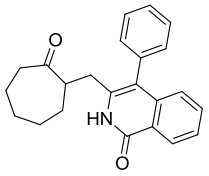
(^{1}H NMR, $CDCl_3$, 500 MHz)



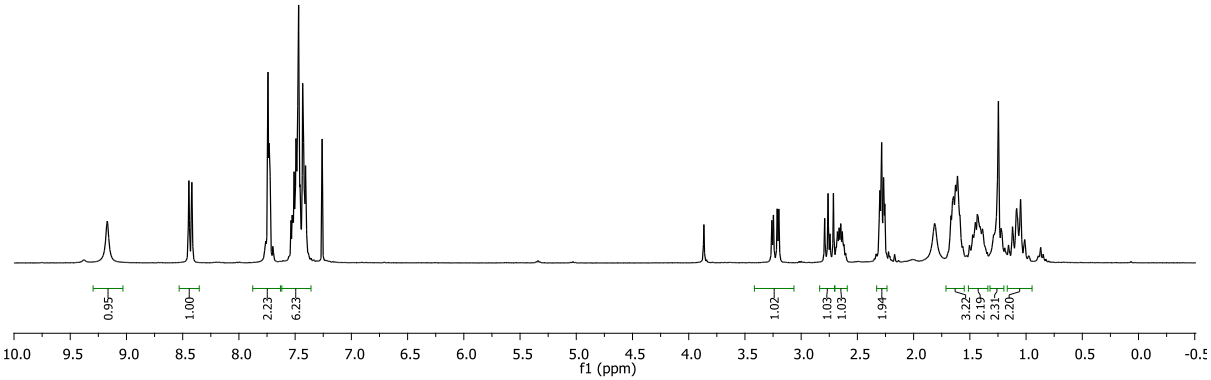


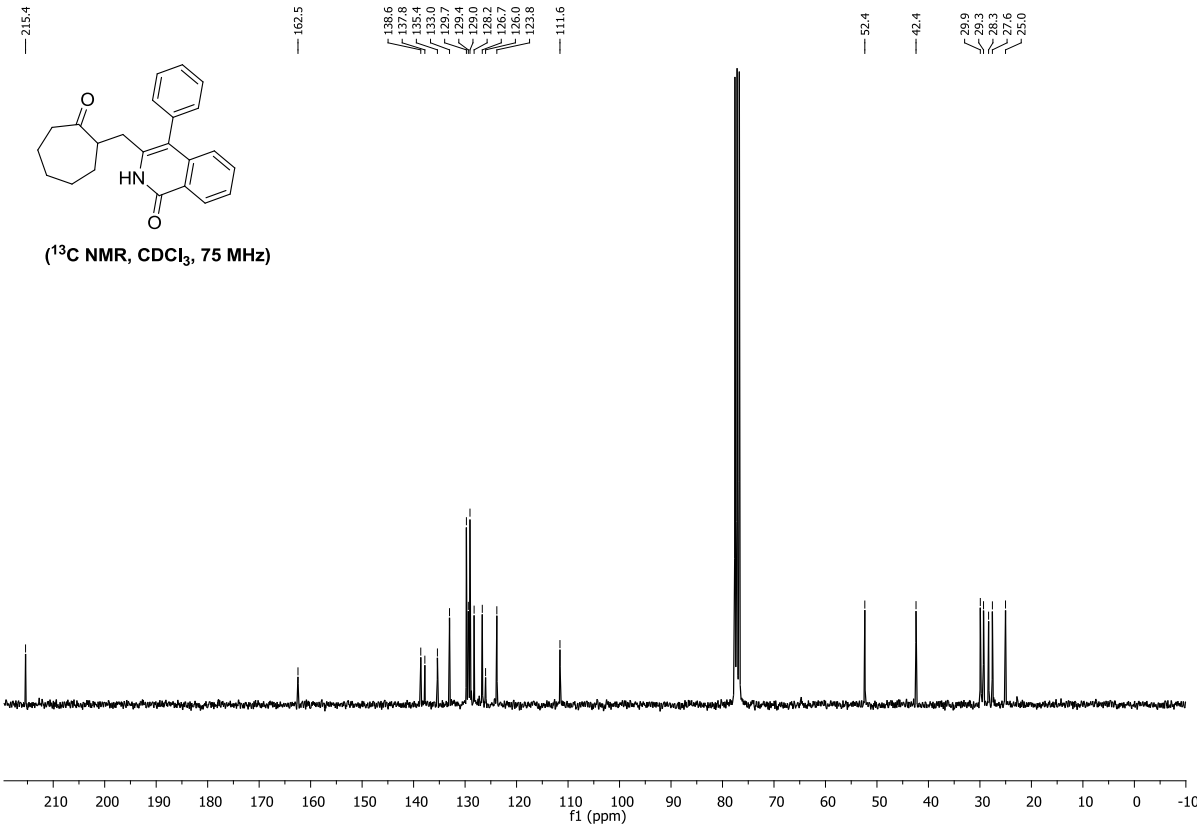
(^{13}C NMR, $CDCl_3$, 125 MHz)

3-((2-oxocycloheptyl)methyl)-4-phenylisoquinolin-1(2H)-one (S5):



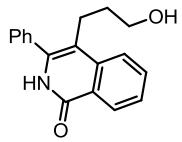
(^{1}H NMR, $CDCl_3$, 300 MHz)



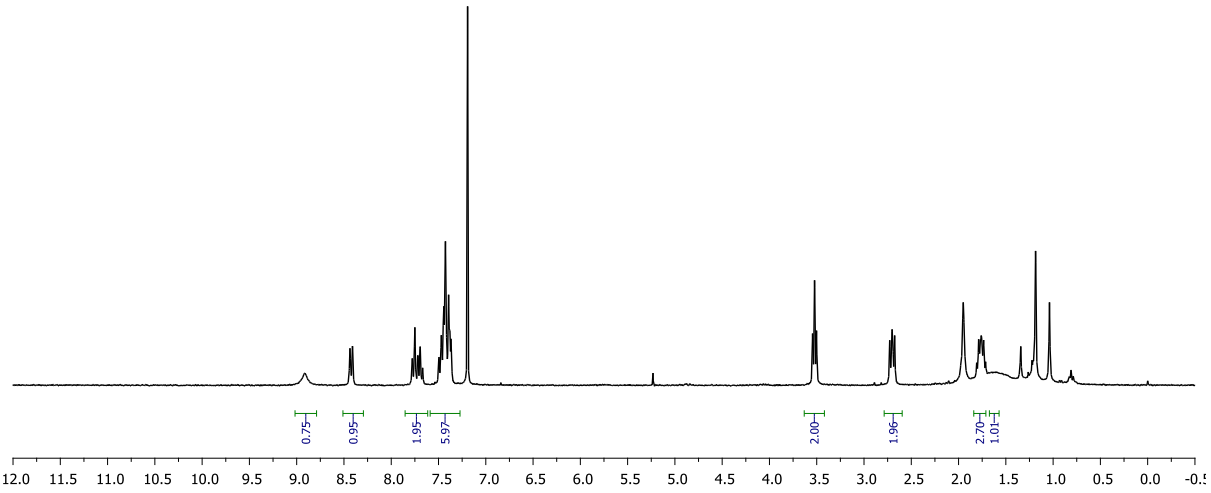


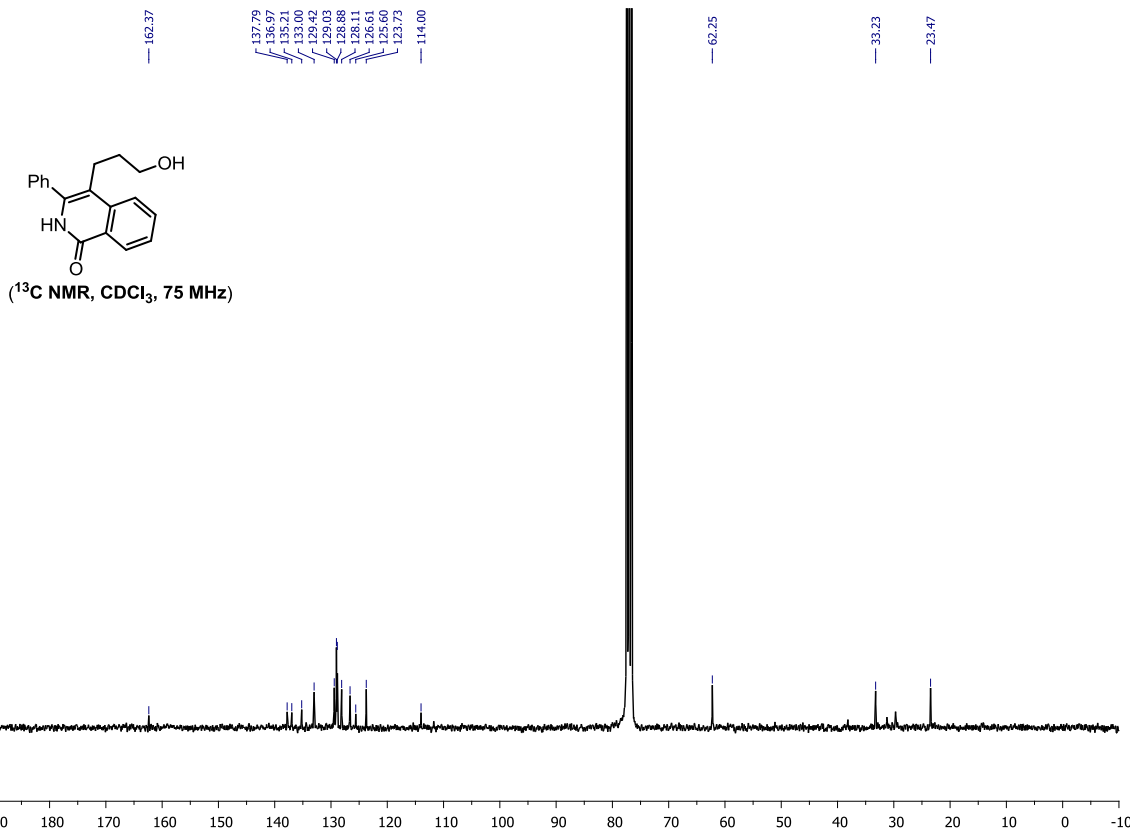
(^{13}C NMR, $CDCl_3$, 75 MHz)

4-(3-Hydroxypropyl)-3-phenylisoquinolin-1(2*H*)-one (7a):



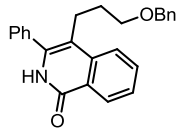
(^{1}H NMR, $CDCl_3$, 300 MHz)



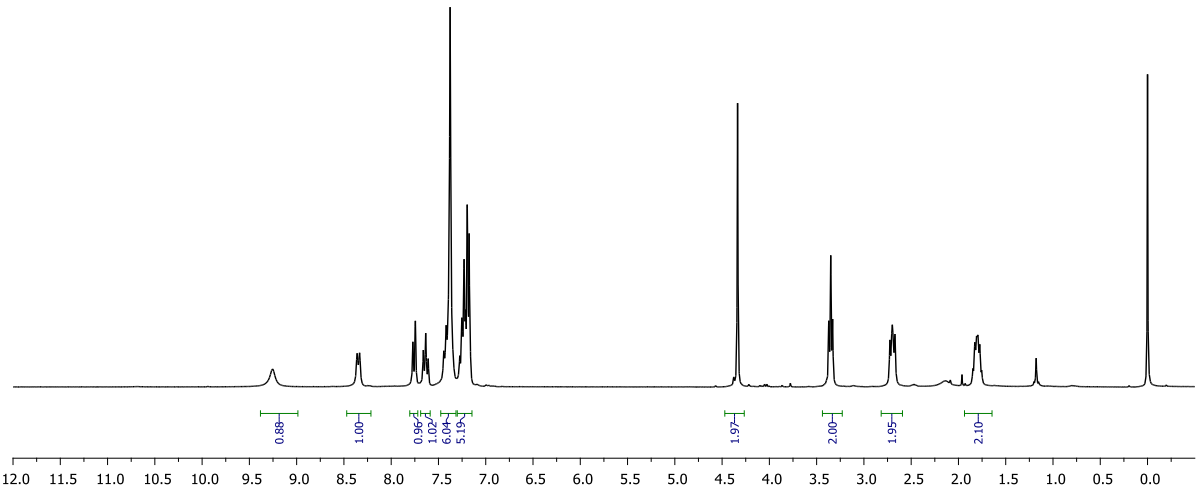


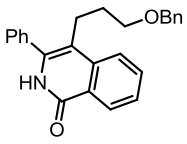
(^{13}C NMR, $CDCl_3$, 75 MHz)

4-(3-(Benzyloxy)propyl)-3-phenylisoquinolin-1(2H)-one (7b):



(^{1}H NMR, $CDCl_3$, 300 MHz)





(^{13}C NMR, $CDCl_3$, 75 MHz)